	Ref #	Hits	Search Text
1	S1	3	(human adj t adj cell adj leukemia adj virus) and crcx4
2	S2	4	cancer and crcx4
3	S3	3	cancer and crcx4 and HTLV
4	S5	1	S4 and cxcr4
5	S4	64	tamamura-h.in.
6	S6	2	"7138488"
7	S7	2	"20060264378"
8	S8	13	crcx4
9	S9	2681	cxcr4
10	S10	474	cxcr4 adj antagonist
11	S11	391	S10 and peptide
12	S12	356	S11 and cyclic
13	S13	0	S12 and (amino adj benzoyl)
14	S14	4	"2002020561"
15	S15	2	"200220561"
16	S16	2	"20060264378"
17	S17	1768	T140
18	S18	293	T140 same cxcr4
19	S19	0	S18 same (chronic adj rheumatoid adj arthritis)
20	S20	0	S18 same (rheumatoid adj arthritis)
21	S21	270	S18 and (rheumatoid adj arthritis)
22	S22	274	T140 same (cxcr4 adj antagonist)
23	S23	270	S22 and (rheumatoid arthritis)
24	S24	57	Fujii-nobutaka.in.
25	S25	4	tamamura-hirokazu.in.
26	S26	60	hori-akira.in.

GenCore version 6.2.1

OM protein - protein search, using sw model

Run on: June 19, 2007, 14:53:54 ; Search time 193 Seconds
(without alignments)
40.566 Million cell updates/sec

Title: US-10-525-838-64
Perfect score: 64
Sequence: 1 XRRXCYXKXPYRXCRX 16

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 2782304 seqs, 489333398 residues

Total number of hits satisfying chosen parameters: 2782304

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_200701:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*
9: geneseqp2005s:*
10: geneseqp2006s:*
11: geneseqp2007s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	61	95.3	14	5	AAU79688	Aau79688 Horseshoe
2	61	95.3	14	5	AAU79701	Aau79701 Horseshoe
3	61	95.3	14	8	ADO57504	Ado57504 Chemokine
4	61	95.3	14	8	ADO57505	Ado57505 Chemokine
5	61	95.3	14	8	ADO57503	Ado57503 Chemokine
6	60	93.8	14	2	AAW79872	Aaw79872 Peptide s

7	60	93.8	14	4	AAG78634	Aag78634	Antiviral
8	60	93.8	14	5	AAU79700	Aau79700	Horseshoe
9	60	93.8	14	5	AAU79694	Aau79694	Horseshoe
10	60	93.8	14	5	AAU79696	Aau79696	Horseshoe
11	60	93.8	14	5	AAU79686	Aau79686	Horseshoe
12	60	93.8	14	8	ADM86837	Adm86837	CXCR4 ant
13	60	93.8	14	8	ADM86856	Adm86856	CXCR4 ant
14	60	93.8	14	8	ADM86861	Adm86861	CXCR4 ant
15	60	93.8	14	8	ADM86892	Adm86892	CXCR4 ant
16	60	93.8	14	8	ADM86866	Adm86866	CXCR4 ant
17	60	93.8	14	8	ADM86843	Adm86843	CXCR4 ant
18	60	93.8	14	8	ADM86881	Adm86881	CXCR4 ant
19	60	93.8	14	8	ADM86891	Adm86891	CXCR4 ant
20	60	93.8	14	8	ADM86865	Adm86865	CXCR4 ant
21	60	93.8	14	8	ADM86887	Adm86887	CXCR4 ant
22	60	93.8	14	8	ADM86889	Adm86889	CXCR4 ant
23	60	93.8	14	8	ADM86851	Adm86851	CXCR4 ant
24	60	93.8	14	8	ADM86882	Adm86882	CXCR4 ant
25	60	93.8	14	8	ADM86835	Adm86835	CXCR4 ant
26	60	93.8	14	8	ADM86853	Adm86853	CXCR4 ant
27	60	93.8	14	8	ADM86867	Adm86867	CXCR4 ant
28	60	93.8	14	8	ADM86857	Adm86857	CXCR4 ant
29	60	93.8	14	8	ADM86858	Adm86858	CXCR4 ant
30	60	93.8	14	8	ADM86869	Adm86869	CXCR4 ant
31	60	93.8	14	8	ADM86870	Adm86870	CXCR4 ant
32	60	93.8	14	8	ADM86888	Adm86888	CXCR4 ant
33	60	93.8	14	8	ADM86883	Adm86883	CXCR4 ant
34	60	93.8	14	8	ADM86864	Adm86864	CXCR4 ant
35	60	93.8	14	8	ADM86886	Adm86886	CXCR4 ant
36	60	93.8	14	8	ADM86890	Adm86890	CXCR4 ant
37	60	93.8	14	8	ADM86836	Adm86836	CXCR4 ant
38	60	93.8	14	8	ADS73474	Ads73474	CXCR4 pep
39	60	93.8	14	8	ADS73473	Ads73473	CXCR4 pep
40	60	93.8	14	8	ADU09108	Adu09108	Template-
41	60	93.8	14	9	ADV87368	Adv87368	CXCR4 bin
42	59	92.2	14	2	AAR85728	Aar85728	Endotoxin
43	59	92.2	14	2	AAR85733	Aar85733	Endotoxin
44	59	92.2	14	2	AAW37625	Aaw37625	Synergist
45	59	92.2	14	2	AAW37611	Aaw37611	Synergist

ALIGNMENTS

RESULT 1
AAU79688
ID AAU79688 standard; peptide; 14 AA.
XX
AC AAU79688;
XX
DT 15-JUL-2002 (first entry)
XX
DE Horseshoe crab modified peptide TA14005 useful in anti-HIV drug.
XX
KW Tachyplesin family; horseshoe crab; human immunodeficiency virus; HIV;
KW CXCR4 ligand-associated disease; acute lymphoma; osteosarcoma;
KW rheumatism; endotoxin; anti-HIV drug; antirheumatic.

GenCore version 6.2.1

OM protein - protein search, using sw model

Run on: June 19, 2007, 14:56:55 ; Search time 347 Seconds
(without alignments)
49.435 Million cell updates/sec

Title: US-10-525-838-64
Perfect score: 64
Sequence: 1 XRRXCYXKXPYRXCRX 16

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 3281787 seqs, 1072124677 residues

Total number of hits satisfying chosen parameters: 3281787

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : UniProt_8.4:*
1: uniprot_sprot:*
2: uniprot_trembl:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	47	73.4	231	2	Q8MY03_BRABE	Q8my03 branchiosto
2	44	68.8	126	2	Q553L5_DICDI	Q553l5 dictyosteli
3	42	65.6	394	2	Q3BNS1_XANC5	Q3bns1 xanthomonas
4	42	65.6	397	2	Q8PG75_XANAC	Q8pg75 xanthomonas
5	41	64.1	788	2	Q8T4K4_CAEEL	Q8t4k4 caenorhabdi
6	41	64.1	788	2	Q9N593_CAEEL	Q9n593 caenorhabdi
7	41	64.1	790	2	Q61H98_CAEBR	Q61h98 caenorhabdi
8	40	62.5	143	2	Q7XHS4_ORYSA	Q7xhs4 oryza sativ
9	39	60.9	175	2	Q8QS87_9BETA	Q8qs87 pongine her
10	39	60.9	371	2	Q17JW6_AEDAE	Q17jw6 aedes aegyp
11	39	60.9	393	2	Q48IV3_PSE14	Q48iv3 pseudomonas
12	39	60.9	393	2	Q881J5_PSESM	Q881j5 pseudomonas
13	39	60.9	393	2	Q4ZSY1_PSEU2	Q4zsy1 pseudomonas
14	39	60.9	398	2	Q4UQ64_XANC8	Q4uq64 xanthomonas
15	39	60.9	398	2	Q8P4K9_XANCP	Q8p4k9 xanthomonas

16	39	60.9	441	2	Q17JW7_AEDAE	Q17jw7 aedes aegyp
17	39	60.9	473	2	Q7PWF5_ANOGA	Q7pwf5 anopheles g
18	38.5	60.2	104	1	PRM2_CALJA	Q28337 callithrix
19	38	59.4	17	1	TAC1_CARRO	P69136 carcinoscor
20	38	59.4	17	1	TAC1_TACGI	P69135 tachypleus
21	38	59.4	17	1	TAC3_TACGI	P18252 tachypleus
22	38	59.4	18	1	PPM1_LIMPO	P14215 limulus pol
23	38	59.4	18	1	PPM2_LIMPO	P14216 limulus pol
24	38	59.4	77	1	TAC1_TACTR	P14213 tachypleus
25	38	59.4	77	1	TAC2_TACTR	P14214 tachypleus
26	38	59.4	86	2	Q7UI77_RHOBA	Q7ui77 rhodopirell
27	38	59.4	93	1	SCR27_ARATH	P82646 arabidopsis
28	38	59.4	156	2	Q5X2L1_LEGPA	Q5x2l1 legionella
29	38	59.4	168	2	Q7EZX8_ORYSA	Q7ezx8 oryza sativ
30	38	59.4	318	2	Q6MYU9_ASPFU	Q6myu9 aspergillus
31	38	59.4	393	2	Q2NIA8_METST	Q2nia8 methanospha
32	38	59.4	397	2	Q9RYF1_DEIRA	Q9ryf1 deinococcus
33	38	59.4	399	2	Q1J3H0_DEIGD	Q1j3h0 deinococcus
34	38	59.4	503	1	PIGW_BOVIN	Q1lza4 bos taurus
35	38	59.4	873	2	Q4N6X6_THEPA	Q4n6x6 theileria p
36	37.5	58.6	179	2	Q5Z706_ORYSA	Q5z706 oryza sativ
37	37	57.8	71	1	CHH1_MACRS	P81206 macrobrachi
38	37	57.8	73	1	CHH_JASLA	P56687 jasus lalan
39	37	57.8	118	2	Q5AP81_CANAL	Q5ap81 candida alb
40	37	57.8	400	2	Q7PZS8_ANOGA	Q7pzs8 anopheles g
41	37	57.8	429	2	Q6FEN0_ACIAD	Q6fen0 acinetobact
42	37	57.8	502	1	PIGW_RAT	Q7tsn4 rattus norv
43	37	57.8	503	1	PIGW_MOUSE	Q8c398 mus musculu
44	37	57.8	504	1	PIGW_HUMAN	Q7z7b1 homo sapien
45	37	57.8	523	2	Q17E45_AEDAE	Q17e45 aedes aegyp

ALIGNMENTS

```
RESULT 1
Q8MY03_BRABE
ID   Q8MY03_BRABE   PRELIMINARY;   PRT;   231 AA.
AC   Q8MY03;
DT   01-OCT-2002, integrated into UniProtKB/TrEMBL.
DT   01-OCT-2002, sequence version 1.
DT   18-APR-2006, entry version 19.
DE   Insulin-like growth factor binding protein (Fragment).
GN   Name=bbIGFBP;
OS   Branchiostoma belcheri (Amphoxius).
OC   Eukaryota; Metazoa; Chordata; Cephalochordata; Branchiostomidae;
OC   Branchiostoma.
OX   NCBI_TaxID=7741;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RA   Kubokawa K.;
RL   Submitted (FEB-2002) to the EMBL/GenBank/DDBJ databases.
CC   ---------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---------------------------------------------------------------------
DR   EMBL; AB080316; BAB97382.1; -; mRNA.
```

GenCore version 6.2.1

OM protein - protein search, using sw model

Run on: June 19, 2007, 14:57:14 ; Search time 21 Seconds
(without alignments)
73.308 Million cell updates/sec

Title: US-10-525-838-64
Perfect score: 64
Sequence: 1 XRRXCYXKXPYRXCRX 16

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 283416 seqs, 96216763 residues

Total number of hits satisfying chosen parameters: 283416

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : PIR_80:*
1: pir1:*
2: pir2:*
3: pir3:*
4: pir4:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	38.5	60.2	104	2	S53118	protamine p2 - com
2	38	59.4	17	2	A38824	tachyplesin I - ho
3	38	59.4	17	2	JX0125	tachyplesin III -
4	38	59.4	18	2	JU0124	polyphemusin I - A
5	38	59.4	18	2	JU0125	polyphemusin II -
6	38	59.4	19	2	JX0124	tachyplesin I prec
7	38	59.4	77	2	A38345	tachyplesin I prec
8	38	59.4	77	2	B38345	tachyplesin II pre
9	38	59.4	397	2	B75592	UDP-galactopyranos
10	37	57.8	1078	2	T42712	myelin transcripti
11	36	56.2	81	2	T14444	pollen coat protei
12	36	56.2	195	2	H71266	hypothetical prote
13	36	56.2	546	2	F84900	hypothetical prote

14	35	54.7	128	2	JN0790	ubiquitin/ribosoma
15	35	54.7	128	2	S34332	ubiquitin / riboso
16	35	54.7	128	2	C48111	ubiquitin / riboso
17	35	54.7	128	2	S34333	ubiquitin / riboso
18	35	54.7	135	2	S48141	hypoglycemic hormo
19	35	54.7	135	2	S48142	hypoglycemic hormo
20	35	54.7	356	1	UQUTRC	polyubiquitin / ri
21	35	54.7	795	2	S26712	hypothetical prote
22	35	54.7	837	2	T19271	hypothetical prote
23	34	53.1	74	2	S10332	ubiquitin / riboso
24	34	53.1	169	2	T51398	hypothetical prote
25	34	53.1	251	2	AC0534	probable hydroxyac
26	34	53.1	251	2	F64745	probable hydroxyac
27	34	53.1	251	2	H90654	probable hydroxyac
28	34	53.1	251	2	H85505	probable hydroxyac
29	34	53.1	255	2	H69968	conserved hypothet
30	34	53.1	296	2	S21306	hypothetical prote
31	34	53.1	527	2	T22867	hypothetical prote
32	33.5	52.3	303	2	B70554	hypothetical prote
33	33.5	52.3	515	2	T08156	RNA maturase (EC 2
34	33	51.6	73	2	S29776	hyperglycemic neur
35	33	51.6	117	2	A32416	phospholipase A2 (
36	33	51.6	118	1	PSSNK1	phospholipase A2 (
37	33	51.6	118	2	C34860	phospholipase A2 (
38	33	51.6	118	2	G34860	phospholipase A2 (
39	33	51.6	118	2	F34860	phospholipase A2 (
40	33	51.6	125	2	S38081	hypothetical prote
41	33	51.6	128	2	T27638	ubiquitin/ribosoma
42	33	51.6	128	2	T37547	ubiquitin fusion p
43	33	51.6	128	2	A29456	ubiquitin / riboso
44	33	51.6	129	2	B48470	ubiquitin / riboso
45	33	51.6	133	2	AE2202	hypothetical prote

ALIGNMENTS

RESULT 1
S53118
protamine p2 - common marmoset
C;Species: Callithrix jacchus (common marmoset)
C;Date: 08-Jul-1995 #sequence_revision 21-Jul-1995 #text_change 09-Jul-2004
C;Accession: S53118
R;Saunders, P.T.K.; Gaughan, J.; Millar, M.R.; Kerr, L.E.; Saxty, B.A.
submitted to the EMBL Data Library, March 1995
A;Reference number: S53118
A;Accession: S53118
A;Status: preliminary
A;Molecule type: mRNA
A;Residues: 1-104 <SAU>
A;Cross-references: UNIPROT:Q28337; UNIPARC:UPI000012CD8B; EMBL:X85371;
NID:g732619; PIDN:CAA59687.1; PID:g732620
C;Superfamily: sperm histone

  Query Match 60.2%; Score 38.5; DB 2; Length 104;
  Best Local Similarity 53.3%; Pred. No. 4.3;
  Matches 8; Conservative 1; Mismatches 5; Indels 1; Gaps 1;

STRUCTURE SEARCH OF CLAIM 1

=> fil reg; d stat que l8
FILE 'REGISTRY' ENTERED AT 10:58:36 ON 20 JUN 2007
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STRUCTURE FILE UPDATES: 19 JUN 2007 HIGHEST RN 937844-74-1
DICTIONARY FILE UPDATES: 19 JUN 2007 HIGHEST RN 937844-74-1

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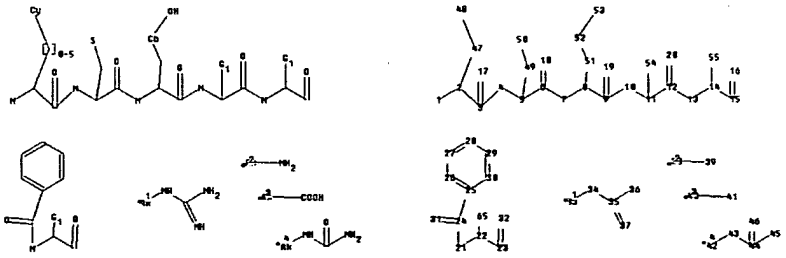
L5 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

Uploading L5.str



chain nodes :
1 2 3 4 16 17 18 19 20 21 22 23 24 31 32 33 34 35 36 37 38 39
40 41 42 43 44 45 46 47 48 51 52 53 54 55 65
ring nodes :
25 26 27 28 29 30
ring/chain nodes :

5 6 7 8 9 10 11 12 13 14 15 49 50
chain bonds :
1-2 2-3 2-47 3-4 3-17 4-5 6-18 8-51 9-19 11-54 12-20 14-55 15-16 21-22
21-24 22-23 22-65 23-32 24-25 24-31 33-34 34-35 35-36 35-37 38-39 40-41
42-43 43-44 44-45 44-46 47-48 51-52 52-53
ring/chain bonds :
5-6 5-49 6-7 7-8 8-9 9-10 10-11 11-12 12-13 13-14 14-15 49-50
ring bonds :
25-26 25-30 26-27 27-28 28-29 29-30
exact/norm bonds :
1-2 3-4 3-17 4-5 5-6 5-49 6-7 6-18 7-8 8-9 9-10 9-19 10-11 11-12 11-
54 12-13 12-20 13-14 14-15 14-55 15-16 21-22 21-24 22-65 23-32 24-31
33-34 34-35 35-36 35-37 38-39 40-41 42-43 43-44 44-45 44-46 47-48 49-50
exact bonds :
2-3 2-47 8-51 22-23 24-25 51-52 52-53
normalized bonds :
25-26 25-30 26-27 27-28 28-29 29-30

G1:CH3,[*1],[*2],[*3],[*4]

Connectivity :
33:2 E exact RC ring/chain 38:2 E exact RC ring/chain 40:2 E exact RC ring/chain
42:2 E exact RC ring/chain
Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS
18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:Atom
26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS
43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:Atom 49:CLASS 50:CLASS
51:CLASS 52:Atom 53:CLASS 54:CLASS 55:CLASS 65:CLASS
Generic attributes :
48:
Saturation : Unsaturated

L8 32 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED 429921 ITERATIONS 32 ANSWERS
SEARCH TIME: 00.00.24

=> fil capl; d que nos l15
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FILE LAST UPDATED: 19 Jun 2007 (20070619/ED)

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=> d que nos l10; d que nos l14
L5 STR
L8 32 SEA FILE=REGISTRY SSS FUL L5
L10 10 SEA FILE=CAPLUS ABB=ON L8

L1 1 SEA FILE=CAPLUS ABB=ON US2005-525838/AP
L5 STR
L8 32 SEA FILE=REGISTRY SSS FUL L5
L10 10 SEA FILE=CAPLUS ABB=ON L8
L11 2098 SEA FILE=CAPLUS ABB=ON FUJII N?/AU
L12 273 SEA FILE=CAPLUS ABB=ON TAMAMURA H?/AU
L13 494 SEA FILE=CAPLUS ABB=ON HORI A?/AU
L14 10 SEA FILE=CAPLUS ABB=ON ((L11 OR L12 OR L13) AND L10) OR (L11 AND L12 AND L13) OR L1

=> s l10,l14
L16 10 (L10 OR L14)

=> d ibib ed abs hitstr l16 1-10; fil prousddr; s l8

L16 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1252719 CAPLUS Full-text
DOCUMENT NUMBER: 146:20336
TITLE: CXCR4 antagonists for wound healing and re-epithelialization
INVENTOR(S): Peled, Amnon; Fujii, Nobutaka
PATENT ASSIGNEE(S): Hadasit Medical Research Services and Development Ltd., Israel; Kyoto University
SOURCE: PCT Int. Appl., 126pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006126188	A2	20061130	WO 2006-IL596	20060521

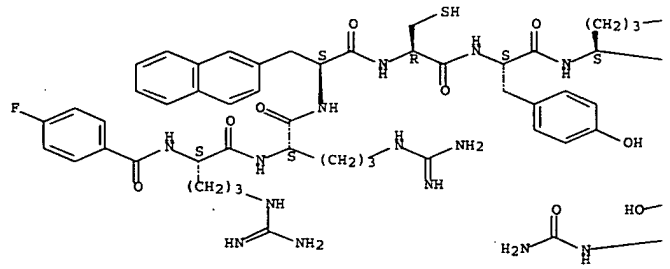
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,

SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-684160P P 20050525
ED Entered STN: 01 Dec 2006
AB The invention provides novel uses for CXCR4 antagonists, including specifically peptides of the T-140 family, in the treatment of skin burns and other injuries. The invention further provides methods and compns. for increasing epithelialization in a subject in need thereof, and for preventing or inhibiting fibrosis and excessive scar formation, using peptide inhibitors of the T-140 family as well as other CXCR4 antagonists.
IT 608143-91-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CXCR4 antagonists for wound healing and re-epithelialization)
RN 608143-91-5 CAPLUS
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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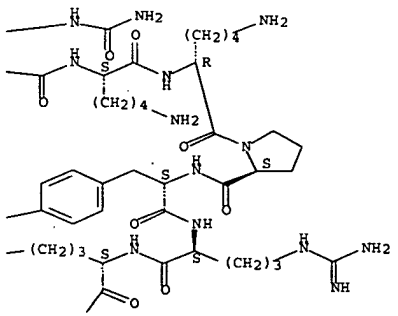

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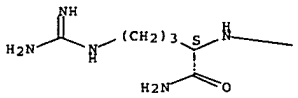

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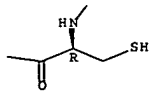


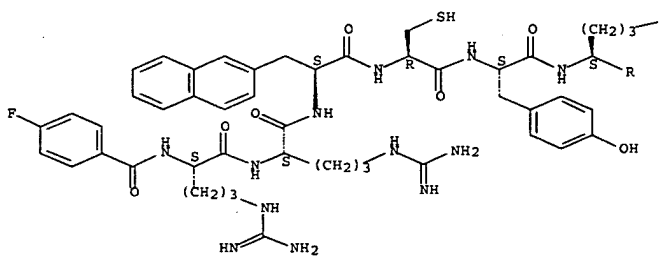
IT 669072-03-1 669072-04-2 669072-22-4
669072-23-5 669072-24-6 669072-25-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CXCR4 antagonists for wound healing and re-epithelialization)

RN 669072-03-1 CAPLUS

CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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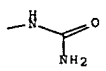

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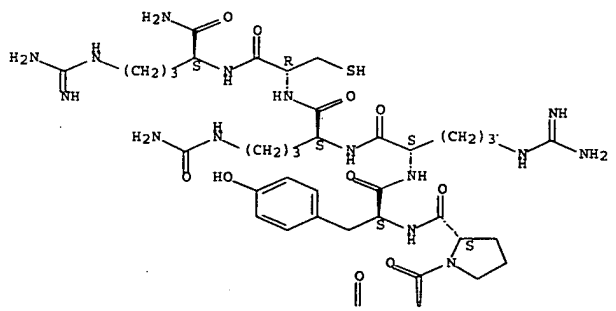

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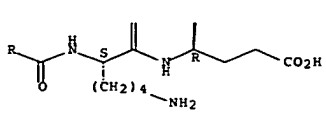

RN 669072-04-2 CAPLUS
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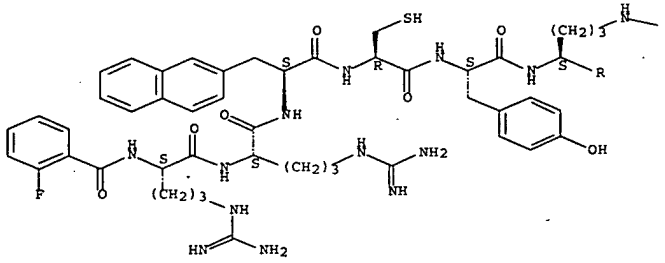
Absolute stereochemistry.

PAGE 1-A



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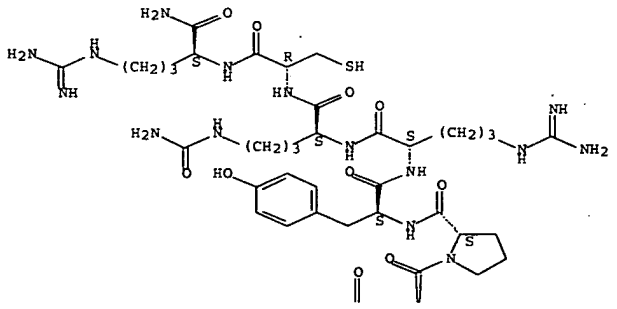
PAGE 2-A



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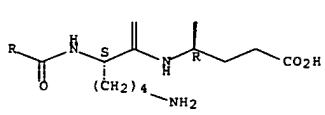

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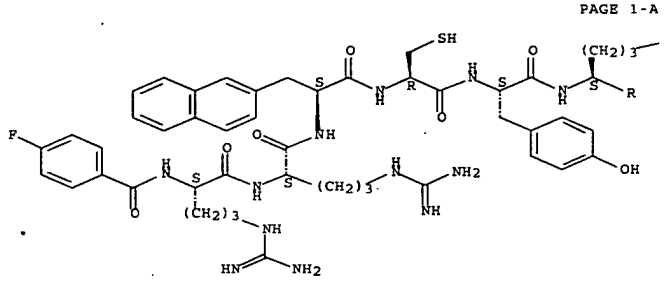
Absolute stereochemistry.

PAGE 1-A



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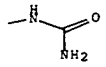

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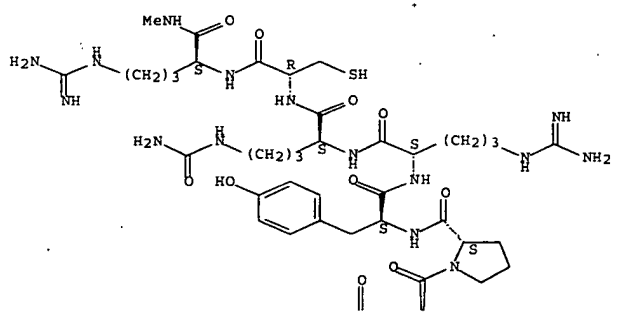

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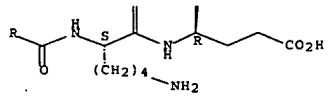

RN 669072-23-5 CAPLUS

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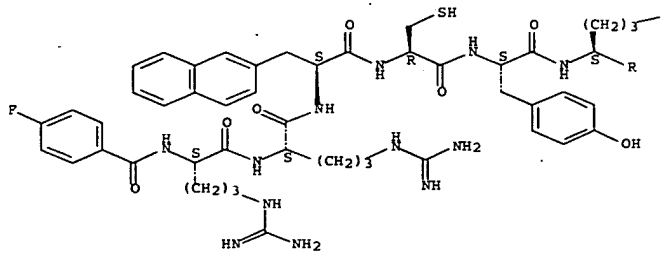
Absolute stereochemistry.

PAGE 1-A



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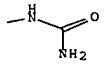

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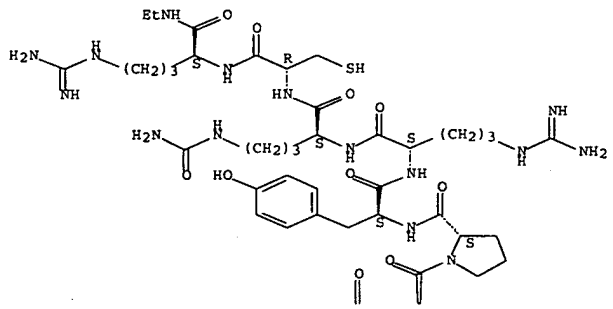

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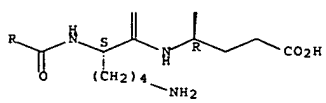

RN 669072-24-6 CAPLUS

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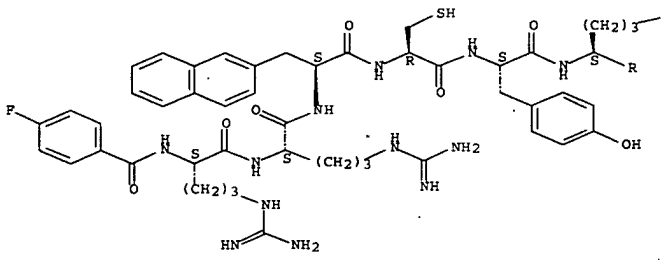
Absolute stereochemistry.

PAGE 1-A



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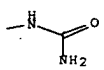

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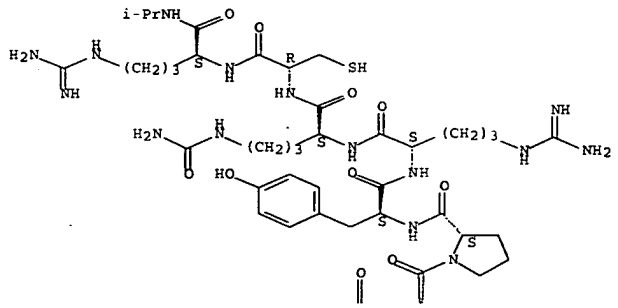

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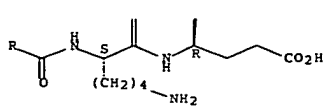

RN 669072-25-7 CAPLUS

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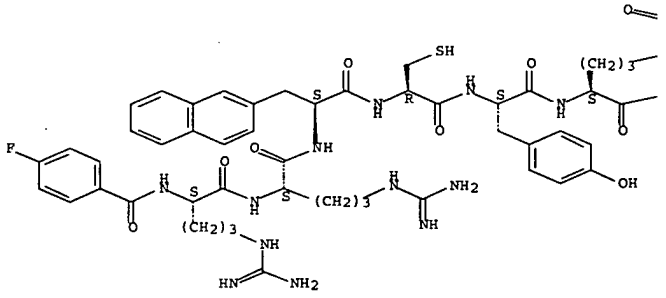
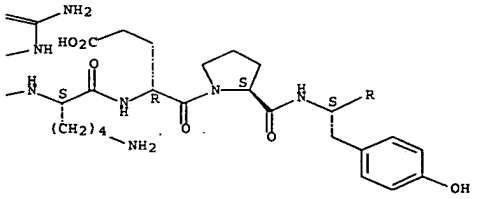
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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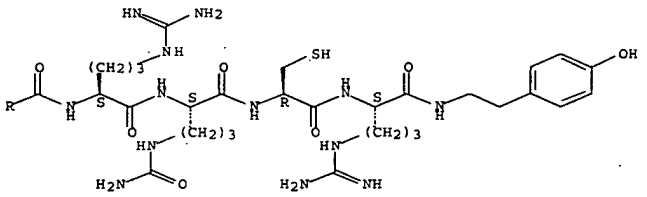


L16 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:560853 CAPLUS Full-text
DOCUMENT NUMBER: 145:486763
TITLE: The involvement of stromal derived factor 1α in homing and progression of multiple myeloma in the 5TMM model
AUTHOR(S): Menu, Eline; Asosingh, Kewal; Indraccolo, Stefano; De Raeve, Hendrik; Van Riet, Ivan; Van Valckenborgh, Els; Vande Broek, Isabelle; Fujii, Nobutaka; Tamamura, Hirokazu; Van Camp, Ben; Vanderkerken, Karin
CORPORATE SOURCE: Dept. of Hematology and Immunology, Vrije Universiteit Brussels, Brussels, Belg.
SOURCE: Haematologica (2006), 91(5), 605-612
CODEN: HAEMAX; ISSN: 0390-6078
PUBLISHER: Ferrata Storti Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 15 Jun 2006
AB Background and Objectives: Multiple myeloma (MM) is a lethal plasma cell cancer characterized by the monoclonal growth of cells in the bone marrow, to reach the bone marrow, MM cells need to be attracted by chemokines. Recently, it has been shown that chemokines can also be involved in the growth of several cancer types. Stromal cell derived factor 1α (SDF1α) or CXCL12 is known to play an important role as a chemokine for hematopoietic progenitor cells and human MM cells. We studied the effects of SDF1α in the 5TMM murine model. Design and Methods: The in vitro effects of SDF1α were analyzed by gelatin zymog., adhesion, migration, proliferation, and chemoinvasion assays and by blockade with the CXCR4 inhibitor, 4F-benzoyl-TN14003. In vivo, diseased mice were treated with either vehicle or 4F-benzoyl-TN14003. Results: In vitro SDF1α was capable of attracting both 5T2MM and 5T33MM cells and inducing a 1.6-fold increase in MMP9 production by the 5TMM cells, which was correlated with an increased invasive capacity. In addition, SDF1α induced a 20% increase in DNA synthesis in the 5TMM cells. All these effects could be blocked by the CXCR4 inhibitor, 4F-benzoyl-TN14003. An in vivo study in the 5T33MM model showed that blocking CXCR4 led to a 20% reduction in bone marrow tumor load. Interpretation and Conclusions: These data demonstrate that SDF1α/CXCR4 is involved in the homing and the expansion of MM cells. Blocking CXCR4 could be useful in synergy with other anti-neoplastic treatments targeting the bone marrow microenvironment.
IT 664334-36-5, 4Fbenzoyl-TN14003
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(SDF1α raised MMP9 production, invasive capacity, DNA synthesis, attracted both 5T2MM and 5T33MM cell, all these effects were blocked by CXR4 inhibitor 4Fbenzoyl-TN14003 in 5TMM cell and reduced bone marrow tumor load in 5T33MM mouse model)
RN 664334-36-5 CAPLUS
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

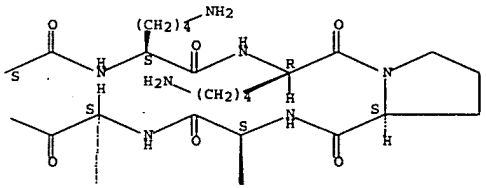
Absolute stereochemistry.

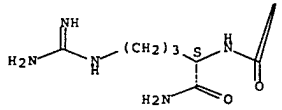
PAGE 1-A

F

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C





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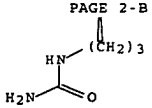

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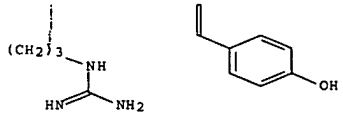


REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1340613 CAPLUS Full-text
DOCUMENT NUMBER: 144:381434
TITLE: Translational Research - from lab to clinic: new HIV-drug inhibits in vitro bladder cancer migration and invasion
AUTHOR(S): Retz, M.; Sidhu, S. S.; Lehmann, J.; Tamamura, H.; Fujii, N.; Basbaum, C.
CORPORATE SOURCE: Biomolecular Sciences Program, Cardiovascular Research Institute, Department of Anatomy, UCSF, San Francisco, CA, 94143-0452, USA
SOURCE: European Urology (2005), 48(6), 1025-1030
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 26 Dec 2005
AB Objective: The CXCR4/CXCL12 axis appears crucial in the metastasis of bladder cancer. Our aim was to evaluate the potency of the CXCR4 antagonist, 4F-benzoyl-TE14011 (4F-bTE), as an anti-metastatic drug in this disease. In this study, we assessed the ability of 4F-bTE to inhibit tumor cell motility, invasion through extracellular matrix (ECM), matrix metalloproteinase (MMP) secretion and cytoskeletal responses to chemokine. Methods: To assess the degree to which cells could migrate and invade ECM under various conditions, we used TCCSUP bladder cancer cells in a Boyden chamber system. To monitor actin polymerization, we stained cells on chamber slides with AlexaFluor 594 phalloidin. To measure matrix- metalloproteinase-2 and -9 (MMP) activity, we used gelatin zymog. To assess the effects of the CXCR4 antagonist 4F-bTE on each of the above parameters, we exposed bladder cancer cells either to chemokine CXCL12, alone, or to both CXCL12 and 4F-bTE. We also monitored cells for apoptotic and necrotic changes during drug treatment. Results: The CXCR4 antagonist 4F-bTE markedly decreased CXCL12-induced bladder cancer cell migration and ECM invasion in Boyden chamber assays. The antagonist also blocked chemokine-induced actin polymerization as well as the induction of

MMP-2 and MMP-9 in these cells. Conclusion: The CXCR4 antagonist 4F-bTE has the potential to inhibit expression of the metastatic phenotype and may provide therapeutic value to patients.

IT 627872-93-9, 4F-Benzoyl-TE14011
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(4F-bTE markedly inhibited chemokine CXCL12-induced bladder cancer cell migration, ECM invasion, actin polymerization, MMP activity in TCCSUP cell line indicated 4F-bTE may inhibit metastatic phenotype, provide therapeutic value to patient)

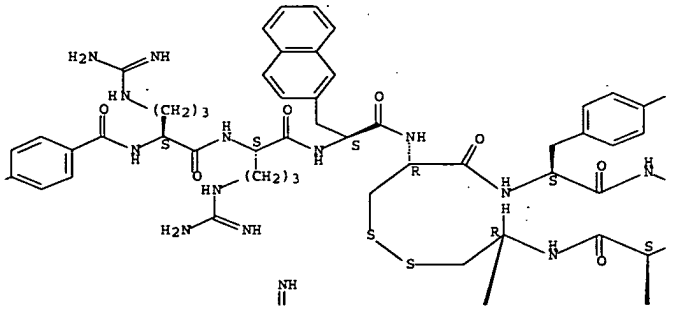
RN 627872-93-9 CAPLUS
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

F

PAGE 1-B



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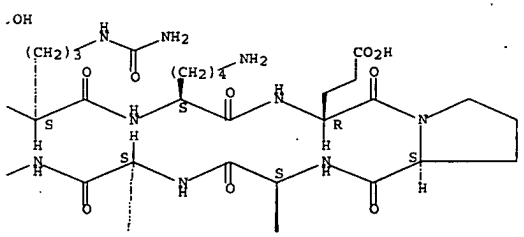
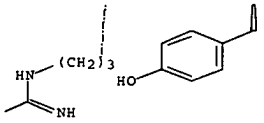


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:575920 CAPLUS Full-text
DOCUMENT NUMBER: 143:259662
TITLE: The chemokine receptor CXCR4 as a therapeutic target for several diseases including AIDS, cancer and rheumatoid arthritis
AUTHOR(S): Tamamura, Hirokazu; Hiramatsu, Kenichi; Ueda, Satoshi; Araki, Takanobu; Takenaga, Mitsuko; Igarashi, Rie; Hori, Akira; Kanzaki, Naoyuki; Fujisawa, Miho; Nakashima, Hideki; Yamamoto, Naoki; Otaka, Akira; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Peptide Science (2005), Volume Date 2004, 41st, 121-122
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Japanese Peptide Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 04 Jul 2005

AB T140-lead CXCR4 antagonists proved to be attractive agents for chemotherapy of HIV infection, cancer metastasis, leukemia, and rheumatoid arthritis, which involve this ligand-receptor system. Thus, CXCR4 represents an important therapeutic target for these diseases. In terms of cancer therapy CXCR4 antagonists might overcome cell adhesion-mediated drug resistance (CAM-DR), which is one of serious problems in the clin. use of anti-cancer drugs.

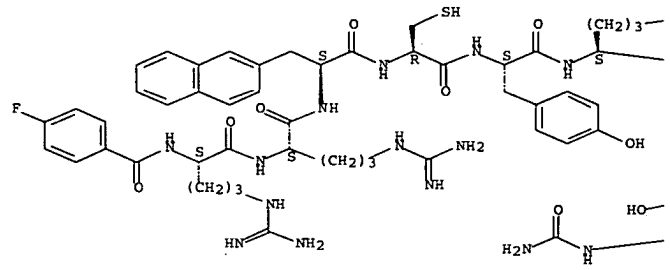
IT 608143-91-5 669072-03-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemokine receptor CXCR4 as chemotherapeutic target for AIDS, cancer, and rheumatoid arthritis)

RN 608143-91-5 CAPLUS

CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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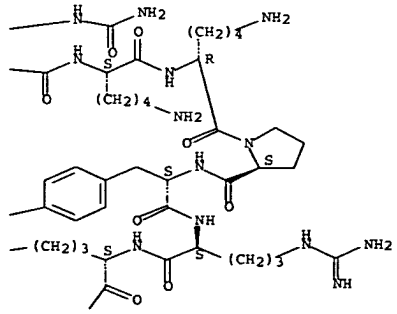

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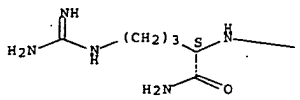

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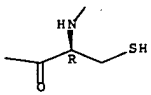

RN 669072-03-1 CAPLUS
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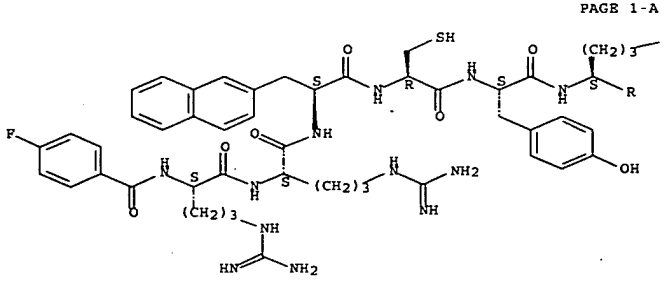
Absolute stereochemistry.

PAGE 1-A



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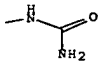

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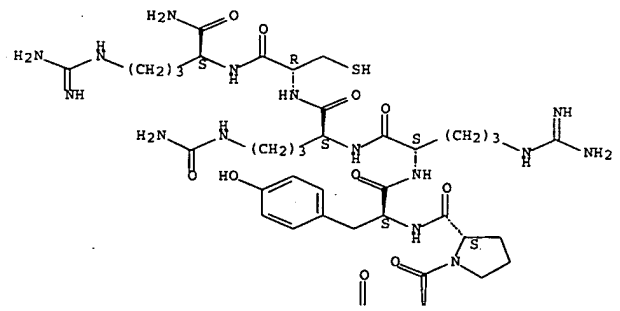

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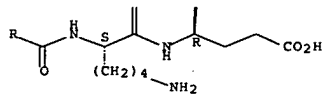


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:314191 CAPLUS Full-text
DOCUMENT NUMBER: 141:235645
TITLE: New leads of low molecular weight CXCR4 antagonists based on enhancement of the T140-based pharmacophores
AUTHOR(S): Mizokami, Satoko; Tamamura, Hirokazu; Hiramatsu, Kenichi; Mizumoto, Makiko; Akamatsu, Miki; Nakashima, Hideki; Wang, Zixuan; Peiper, Stephen C.; Yamamoto, Naoki; Otaka, Akira; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Peptide Science (2003), Volume Date 2004, 40th, 285-288
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Japanese Peptide Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Apr 2004
AB A CXCR4 antagonistic peptide, T140, and its analogs, such as Ac-TE14011, inhibit the entry of T cell line-tropic strains of HIV-1 (X4-HIV-1) into T cells. Herein, a series of TE14011 analogs having modifications with Nα-acylation by several benzoic acid derivs. in the N-terminal region were

synthesized to develop effective compds. with increased biostability. Among these analogs, 4F-benzoyl-TE14011 showed the strongest anti-HIV activity due to CXCR4-antagonism. Structure-activity relation (SAR) studies on TE14011 analogs have disclosed a significant relation between the anti-HIV activity and the Hammett constant (σ) of substituted benzoic acids, suggesting that a 4-fluorobenzoyl moiety at the N-terminus of T140 analogs constitutes a novel T140-based pharmacophore for CXCR4 antagonism. Furthermore, identification of a T140-based new pharmacophore led to development of novel low-mol.-weight CXCR4 antagonists.

IT 627872-93-9 664334-34-3 664334-37-6
664334-38-7 664334-39-8 664334-40-1
664334-41-2 664334-42-3 664334-43-4
664334-44-5 664334-45-6 664334-46-7
664334-47-8 664334-48-9 664334-49-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leads of low mol. weight CXCR4 antagonists based on enhancement of T140-based pharmacophores)

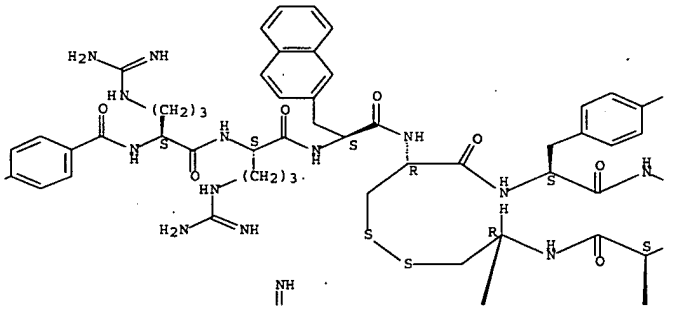
RN 627872-93-9 CAPLUS

CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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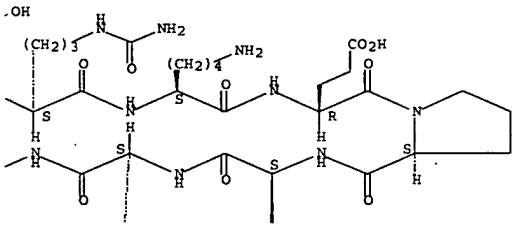

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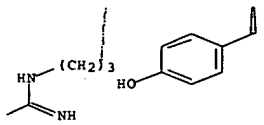

RN 664334-34-3 CAPLUS
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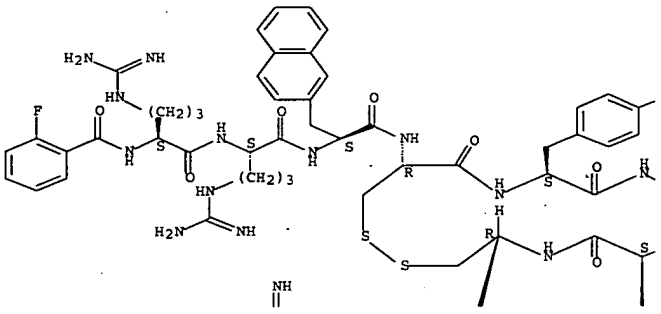
Absolute stereochemistry.

PAGE 1-A



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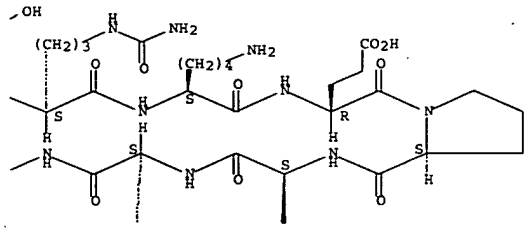

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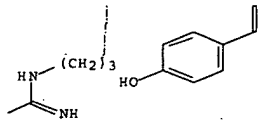
PAGE 2-B



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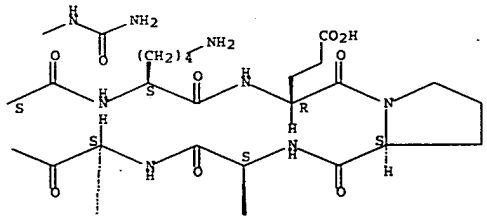
Absolute stereochemistry.

PAGE 1-A

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C



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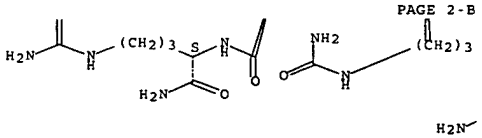

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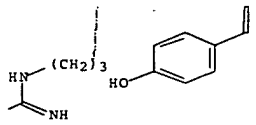

RN 664334-38-7 CAPLUS

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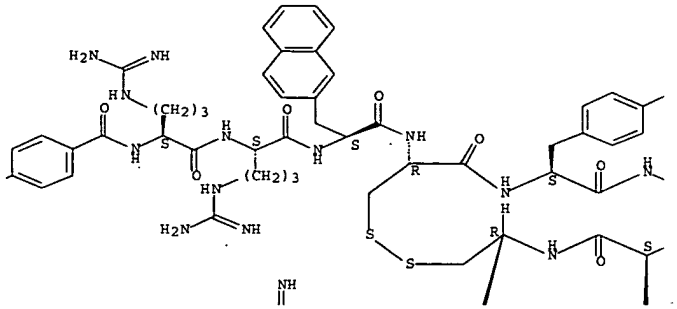
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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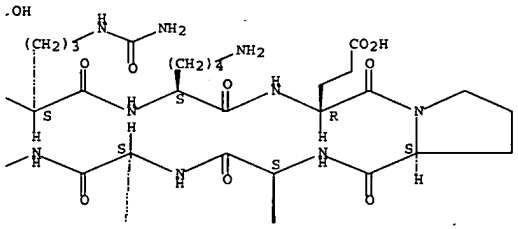

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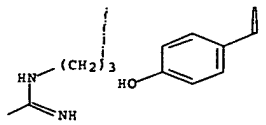

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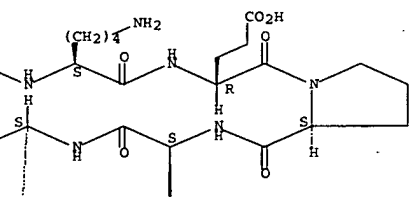
Absolute stereochemistry.

PAGE 1-A



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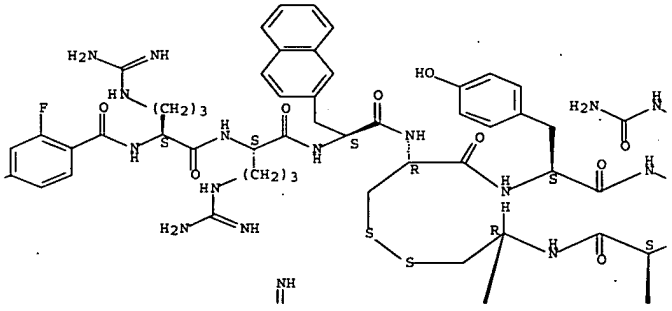

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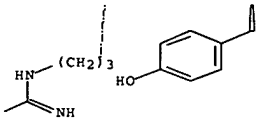
PAGE 2-C



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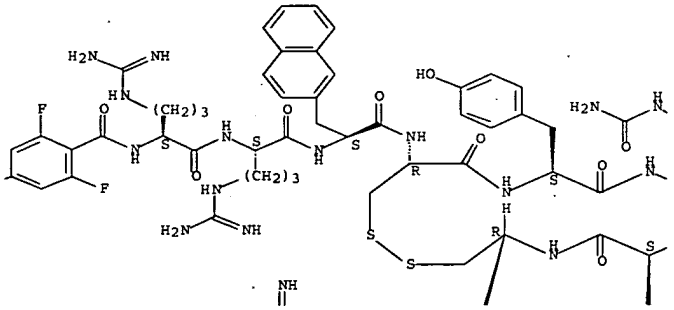
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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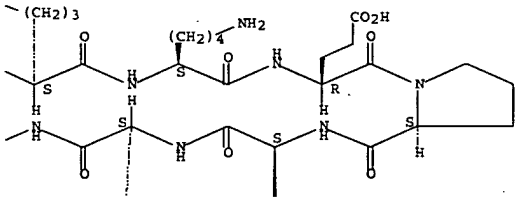

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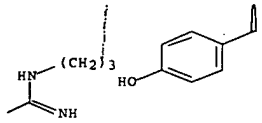

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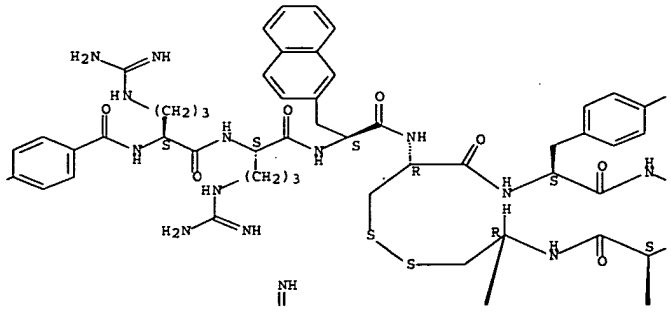
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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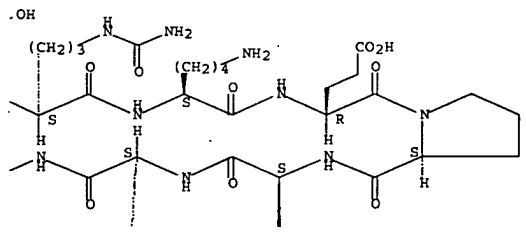
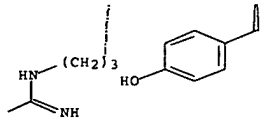


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



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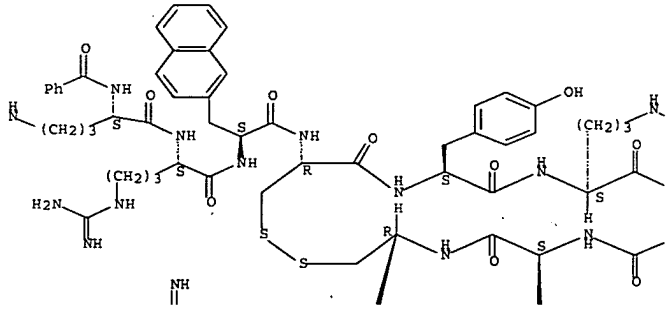
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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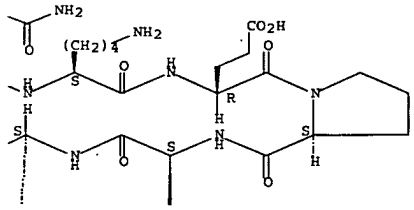

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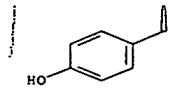

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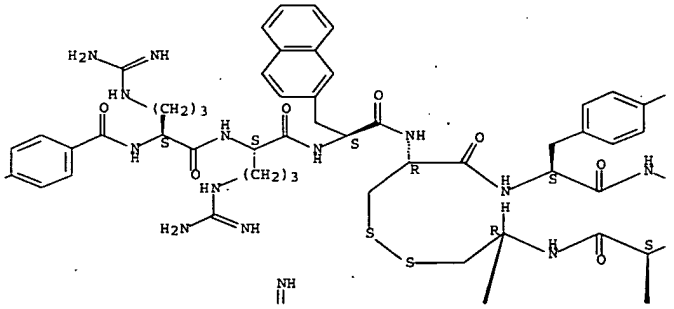
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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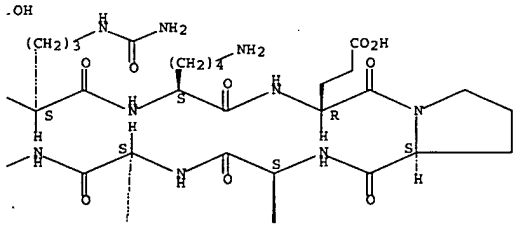
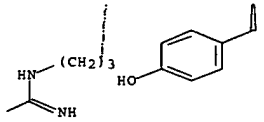


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



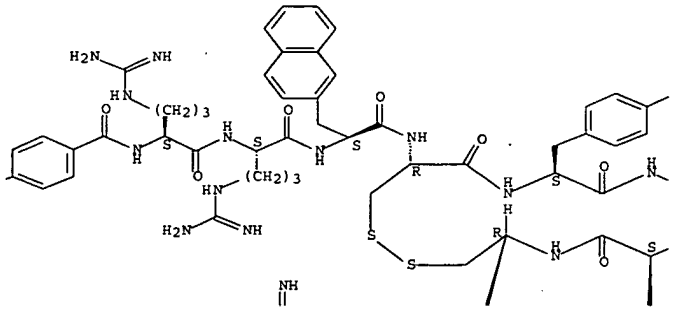
RN 664334-44-5 CAPLUS

CN L-Argininamide, N2-(4-aminobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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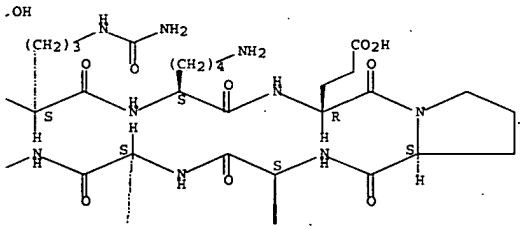
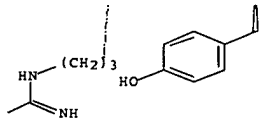


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



RN 664334-45-6 CAPLUS

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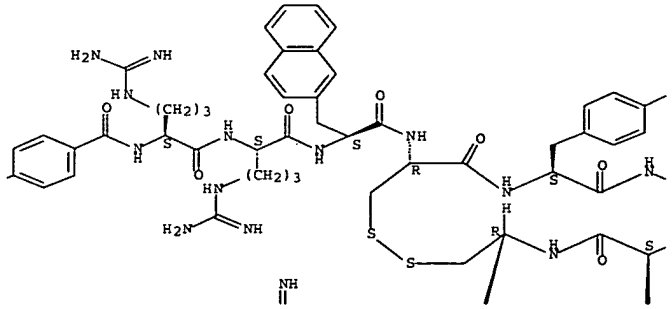
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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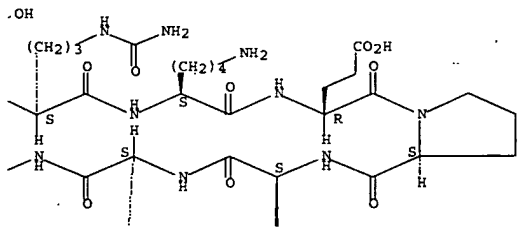
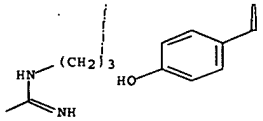


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



RN 664334-46-7 CAPLUS
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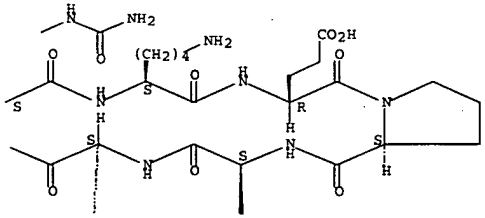
Absolute stereochemistry.

PAGE 1-A

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C



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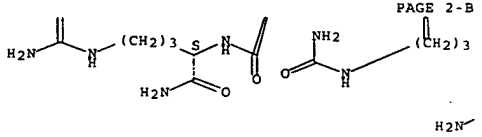

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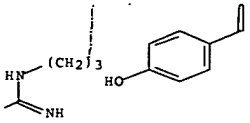

RN 664334-47-8 CAPLUS
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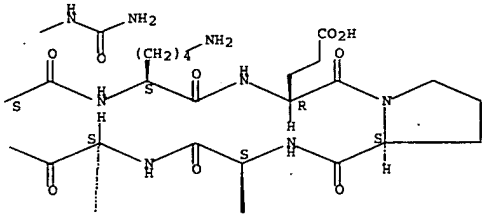
Absolute stereochemistry.

PAGE 1-A

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C



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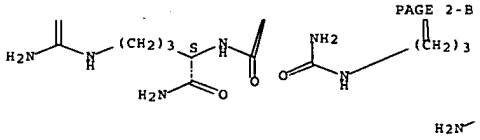

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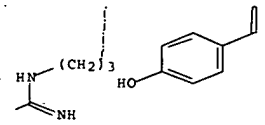

RN 664334-48-9 CAPLUS

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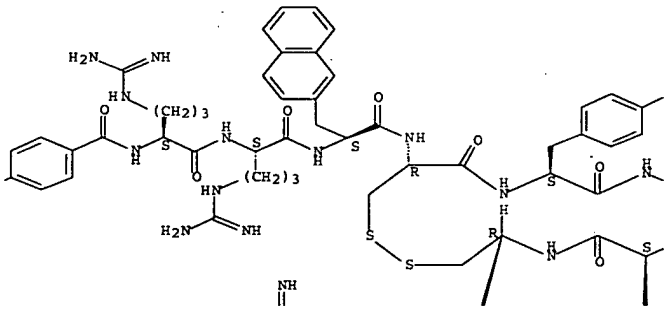
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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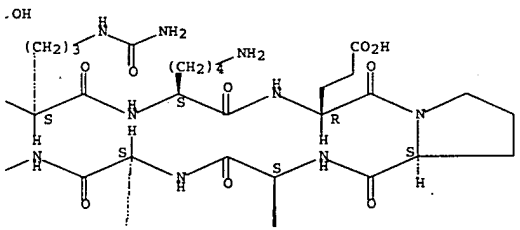
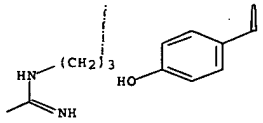


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



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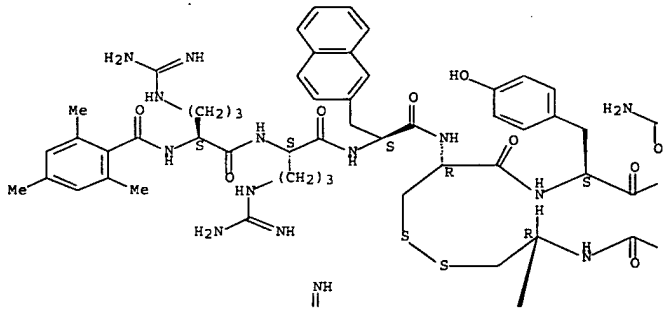
Absolute stereochemistry.

PAGE 1-A



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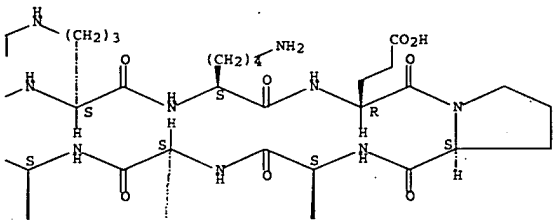

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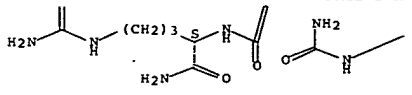

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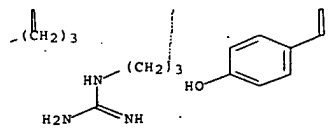


REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:314083 CAPLUS Full-text
DOCUMENT NUMBER: 141:253881
TITLE: CXCR4 antagonists identified as anti-cancer-metastatic agents
AUTHOR(S): Tamamura, Hirokazu; Hori, Akira; Kanzaki, Naoyuki; Hiramatsu, Kenichi; Mizumoto, Makiko; Nakashima, Hideki; Yamamoto, Naoki; Otaka, Akira; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Peptide Science (2003), Volume Date 2004, 40th, 65-68
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Japanese Peptide Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Apr 2004
AB CXCR4 antagonistic peptides, T140 analogs, inhibit the entry of T cell line-tropic strains of HIV-1 (X4-HIV-1) into T cells. Herein, we report that these compds. effectively inhibited stromal cell-derived factor-1 (SDF-1/CXCL12)-induced migration of human leukemia T. cells (Sup-T1) and human breast cancer cells (MDA-MB-231) in vitro. Furthermore, slow release administration by s.c. injection using an Alzet osmotic pump of a potent and bio-stable T140 analog, 4F-benzoyl-TN14003, was found to significantly reduce pulmonary metastasis of MDA-MB-231 in SCID mice. These results suggest that T140 analogs have potential use not only for AIDS therapy but also for cancer therapy.
IT 664334-36-5, 4F-Benzoyl-TN14003
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CXCR4 antagonists as anti-cancer-metastatic agents)
RN 664334-36-5 CAPLUS
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

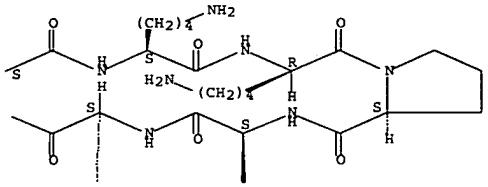
Absolute stereochemistry.

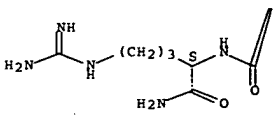
PAGE 1-A

F

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C





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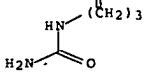

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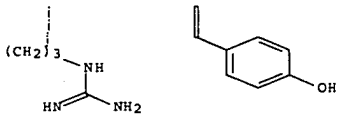


REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:203852 CAPLUS Full-text
DOCUMENT NUMBER: 140:247032
TITLE: CXCR4 antagonist and use thereof
INVENTOR(S): Fujii, Nobutaka; Tamamura, Hirokazu ; Hori, Akira
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

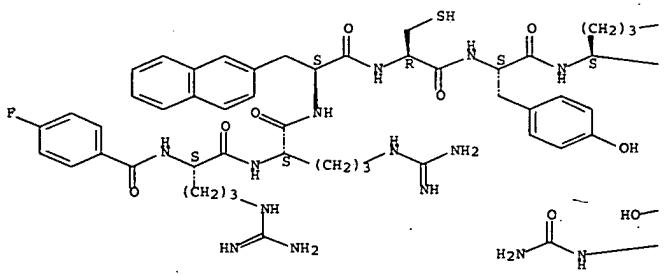
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020462	A1	20040311	WO 2003-JP10753	20030826
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2537158	A1	20040311	CA 2003-2537158	20030826
AU 2003261723	A1	20040319	AU 2003-261723	20030826
JP 2004107333	A	20040408	JP 2003-301176	20030826
EP 1541585	A1	20050615	EP 2003-791288	20030826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006264378	A1	20061123	US 2005-525838	20051014 <--
PRIORITY APPLN. INFO.:			JP 2002-247843 A	20020827
			WO 2003-JP10753 W	20030826

ED Entered STN: 14 Mar 2004
AB It is intended to provide a preventive and/or a remedy for cancer and rheumatoid arthritis which contains a peptide having a CXCR4 antagonism, its amide, its ester or its salt. Also, a novel peptide having a CXCR4 antagonism, its amide, its ester and its salt are provided.
IT 608143-91-5P 669072-03-1P 669072-04-2P
669072-22-4P 669072-23-5P 669072-24-6P
669072-25-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(CXCR4 antagonist and use thereof)
RN 608143-91-5 CAPLUS
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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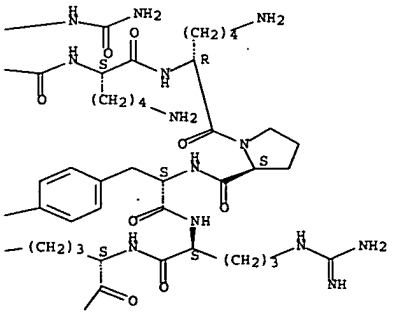

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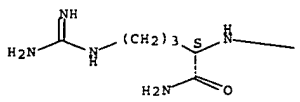

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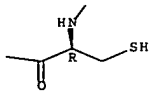

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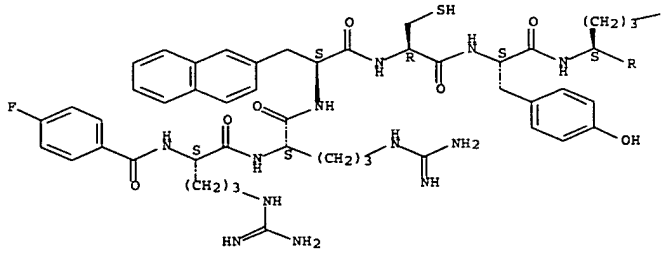
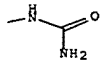
Absolute stereochemistry.

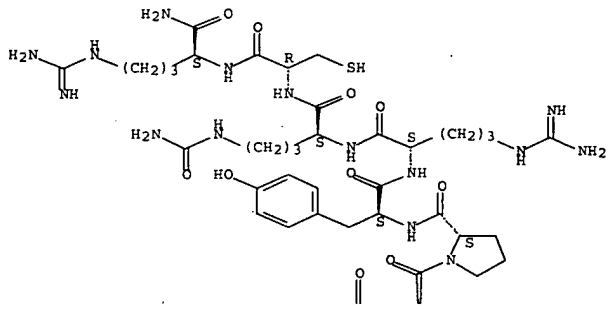
PAGE 1-A



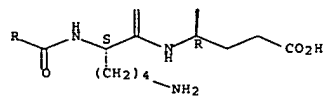
PAGE 1-B



PAGE 2-A



PAGE 3-A



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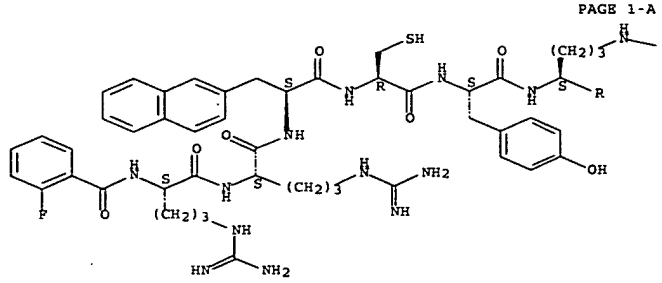
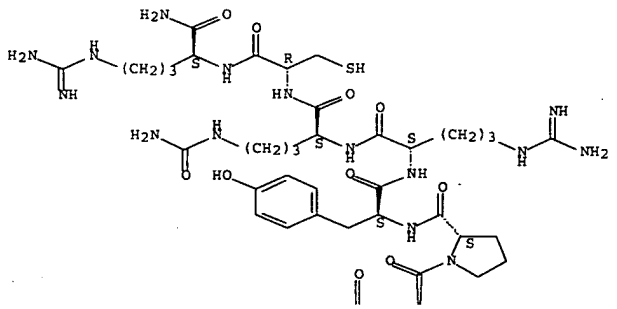
Absolute stereochemistry.

PAGE 1-A

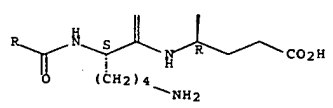


PAGE 1-B

PAGE 2-A



PAGE 3-A



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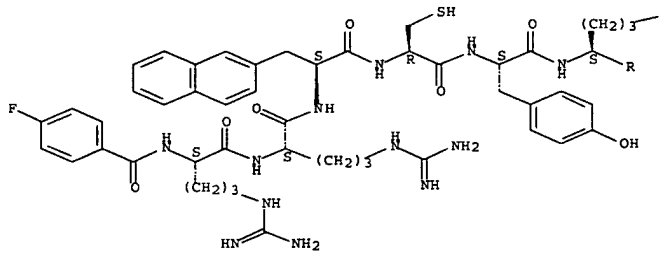
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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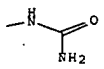

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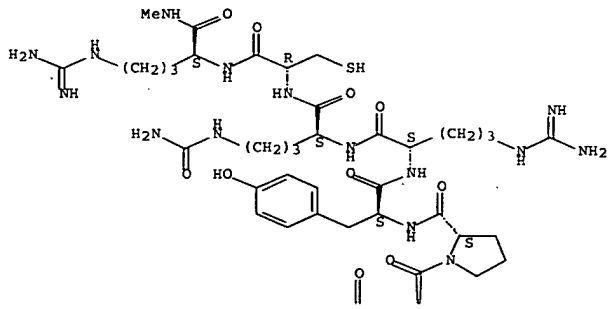

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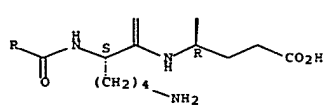

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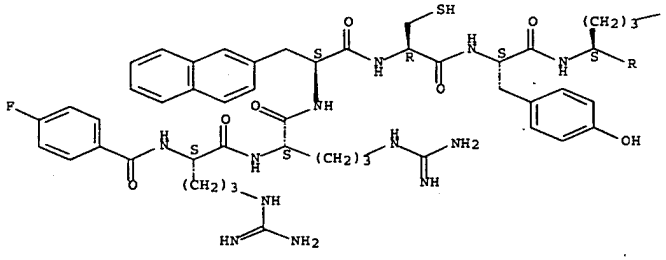
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-N-ethyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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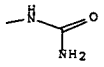

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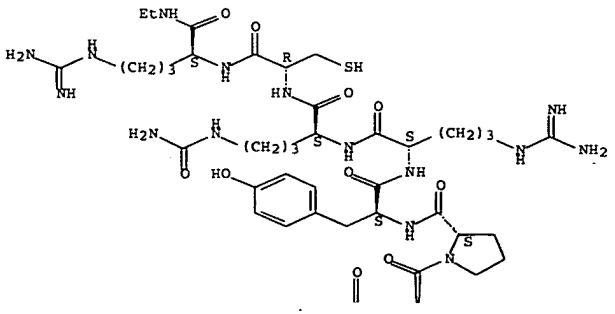

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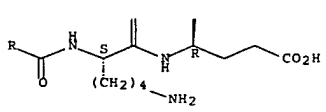

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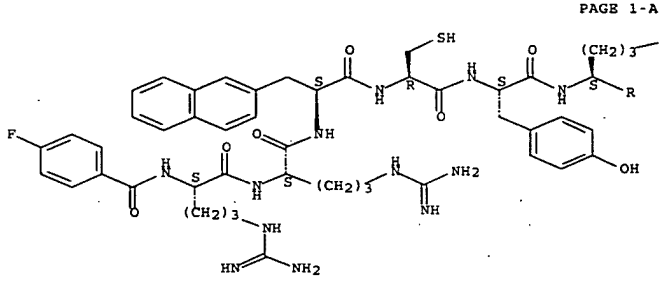
Absolute stereochemistry.

PAGE 1-A



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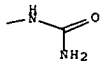

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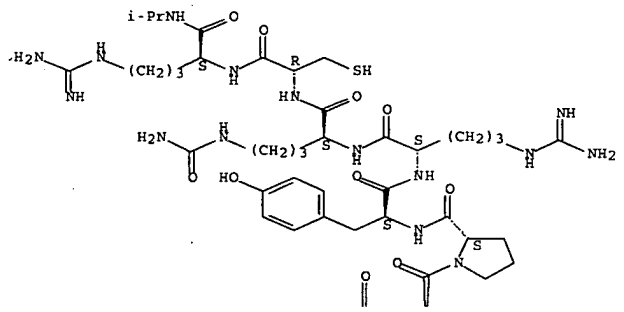

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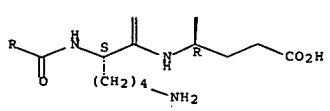

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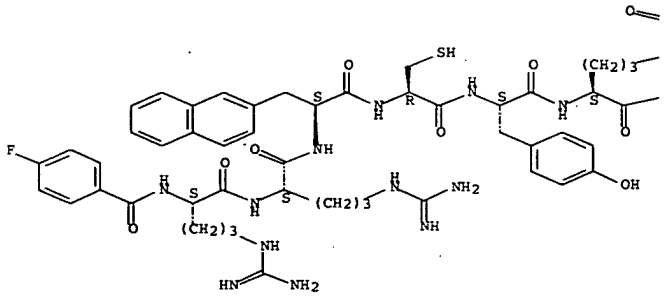
Absolute stereochemistry.

PAGE 1-A



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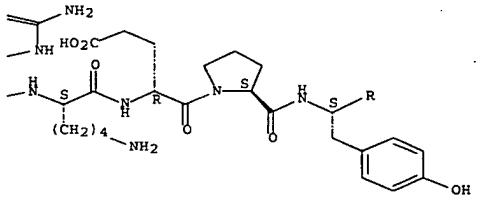

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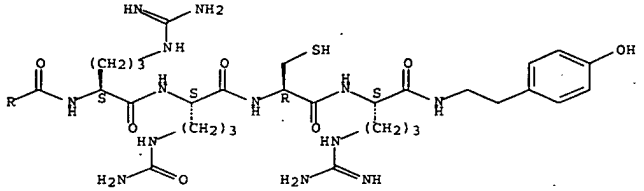


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:833174 CAPLUS Full-text
DOCUMENT NUMBER: 140:209914
TITLE: Enhancement of the T140-based pharmacophores leads to the development of more potent and bio-stable CXCR4 antagonists
AUTHOR(S): Tamamura, Hirokazu; Hiramatsu, Kenichi; Mizumoto, Makiko; Ueda, Satoshi; Kusano, Shuichi; Terakubo, Shigemi; Akamatsu, Miki; Yamamoto, Naoki; Trent, John O.; Wang, Zixuan; Peiper, Stephen C.; Nakashima, Hideki; Otaka, Akira; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Organic & Biomolecular Chemistry (2003), 1(21), 3663-3669
CODEN: OBCRAK; ISSN: 1477-0520
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:209914
ED Entered STN: 24 Oct 2003

AB A CXCR4 antagonistic peptide, T140, and its bio-stable analogs, such as Ac-TE14011, were previously developed. These peptides inhibit the entry of T cell line-tropic strains of HIV-1 (X4-HIV-1) into T cells. Herein, a series of TE14011 analogs having modifications in the N-terminal region were synthesized to develop effective compds. with increased biostability. Among these analogs, 4F-benzoyl-TE14011 (TF14013) showed the strongest anti-HIV activity derived from CXCR4-antagonism, suggesting that a 4-fluorobenzoyl moiety at the N-terminus of T140 analogs constitutes a novel T140-based pharmacophore for CXCR4 antagonists. Structure-activity relationship (SAR) studies on TE14011 analogs with Nα-acylation by several benzoic acid derivs. have disclosed a significant relationship between the anti-HIV activity and the Hammett constant (σ) of substituted benzoic acids. TF14013 was found to be stable in mouse serum, but not completely stable in rat liver homogenate due to deletion of the C-terminal Arg14-NH2 from the parent peptide. This biodegrdn. was completely suppressed by N-alkyl-amidation at the C-terminus. Taken together, the enhancement of the T140-based pharmacophores led to development of a novel CXCR4 antagonist, 4F-benzoyl-TE14011-Me (TF14013-Me), which has very high anti-HIV activity and increased biostability.

IT 627872-93-9P 627872-96-2P 627872-97-3P
627872-98-4P 627872-99-5P 664334-34-3P
664334-36-5P 664334-37-6P 664334-38-7P
664334-39-8P 664334-40-1P 664334-41-2P
664334-42-3P 664334-43-4P 664334-44-5P
664334-45-6P 664334-46-7P 664334-47-8P
664334-48-9P 664334-49-0P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(development of more potent and bio-stable CXCR4 antagonists by enhancement of T140-based pharmacophores)

RN 627872-93-9 CAPLUS .

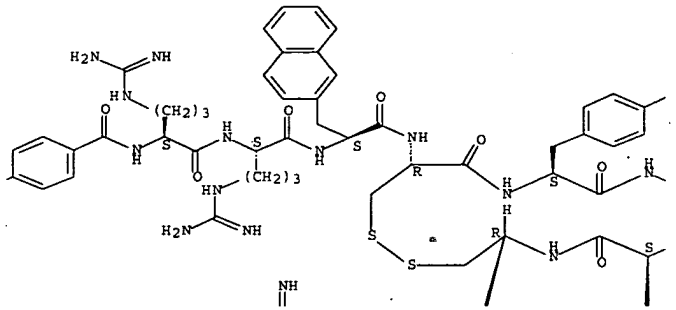
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

F

PAGE 1-B



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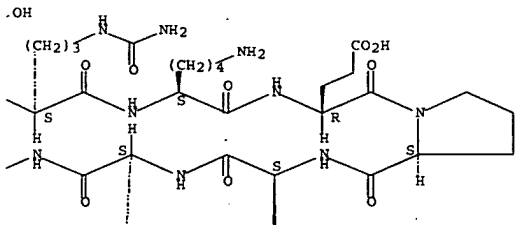

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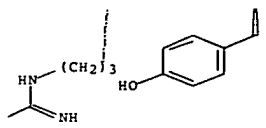
PAGE 2-C



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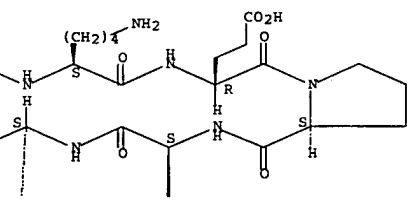
Absolute stereochemistry.

PAGE 1-A



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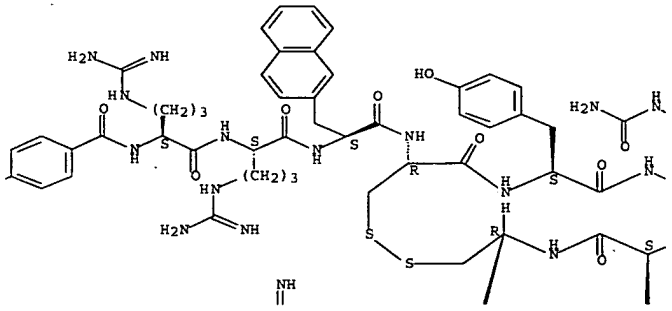

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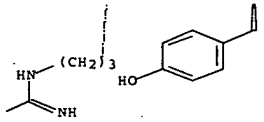
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



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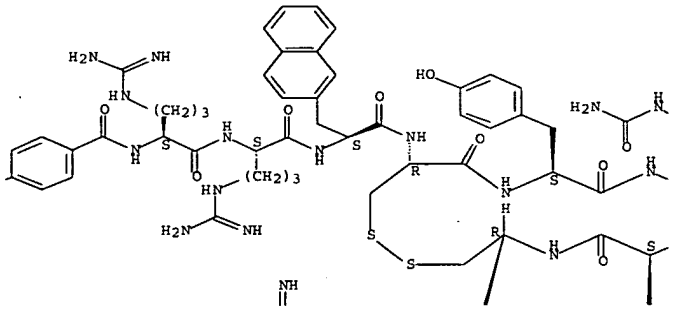
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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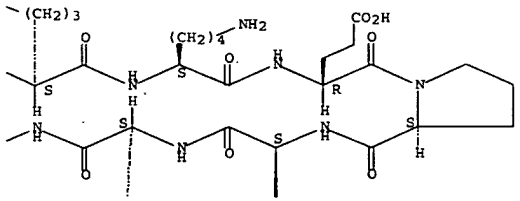

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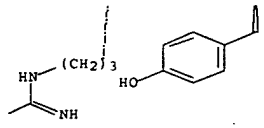

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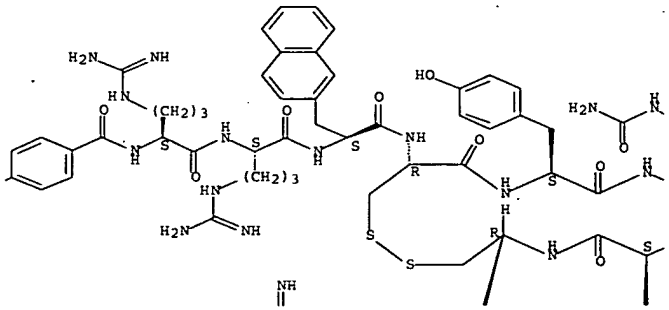
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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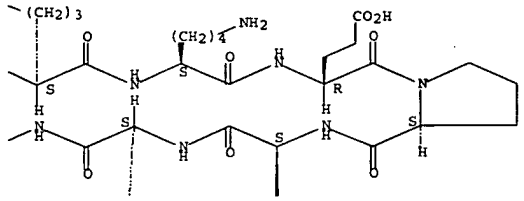

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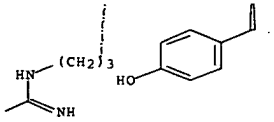
PAGE 2-C



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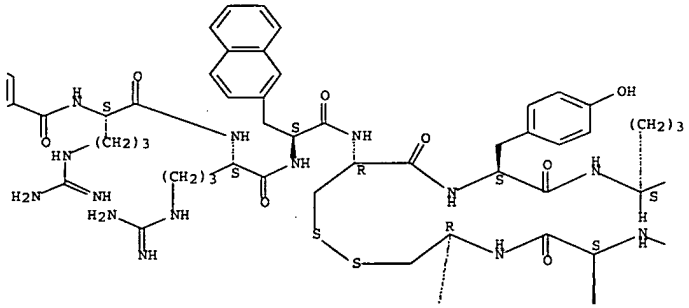
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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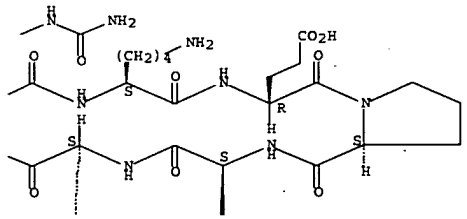

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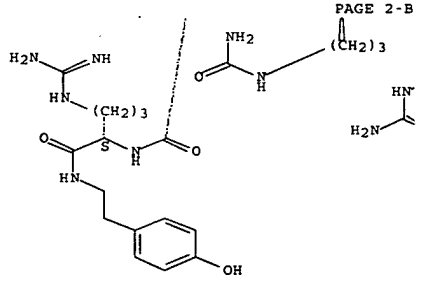

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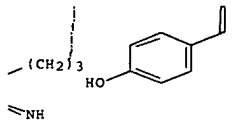

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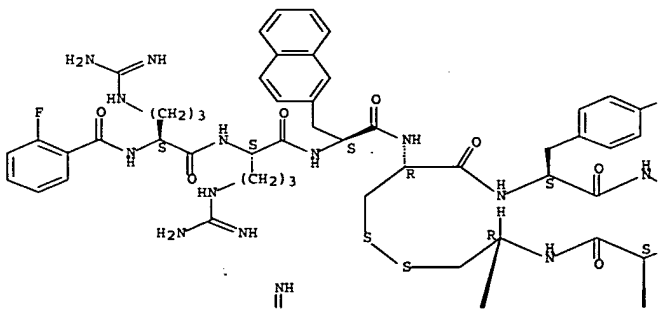
Absolute stereochemistry.

PAGE 1-A



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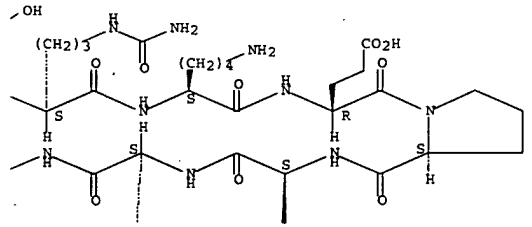

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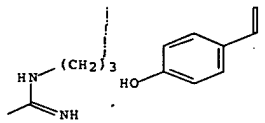

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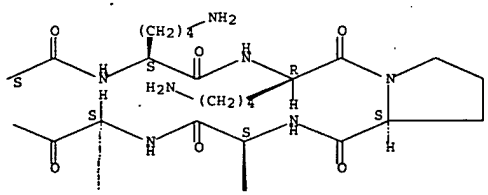
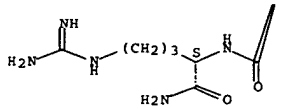
Absolute stereochemistry.

PAGE 1-A

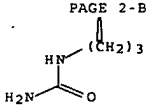
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C





PAGE 2-B



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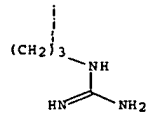
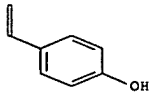




RN 664334-37-6 CAPLUS

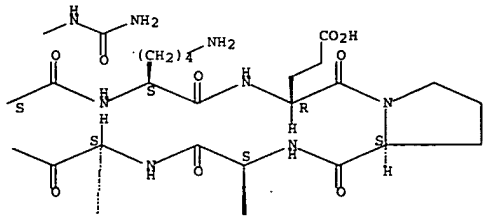
CN L-Argininamide, N2-(4-chlorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C



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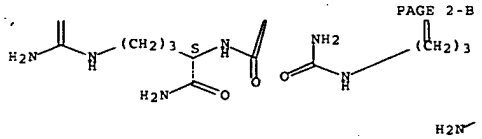
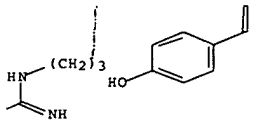


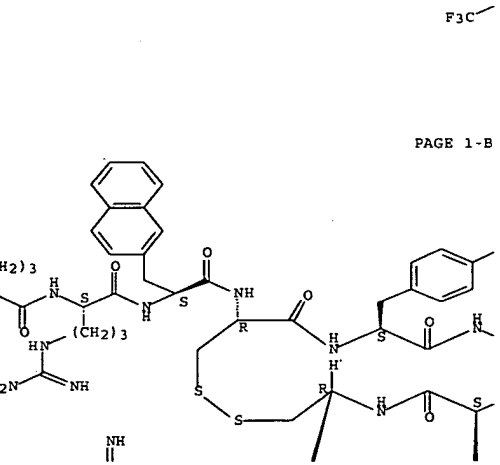
PAGE 2-C



RN 664334-38-7 CAPLUS
CN L-Argininamide, N2-[4-(trifluoromethyl)benzoyl]-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

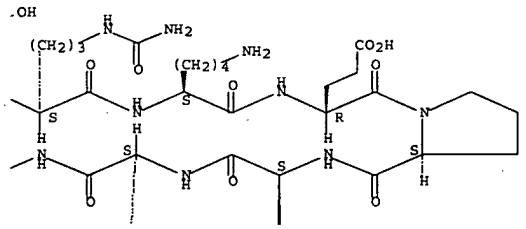
Absolute stereochemistry.

PAGE 1-A



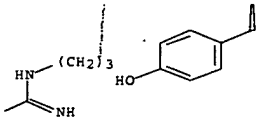
PAGE 1-B

PAGE 1-C



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C

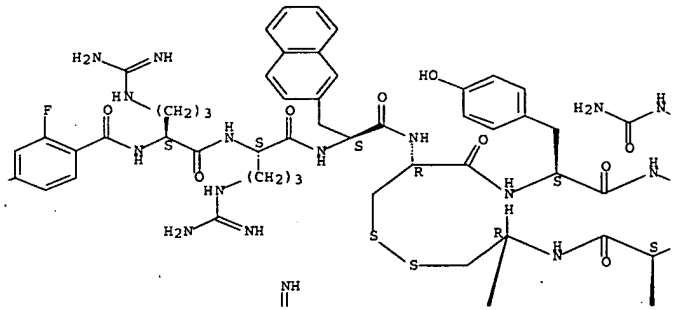


RN 664334-39-8 CAPLUS
CN L-Argininamide, N2-(2,4-difluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

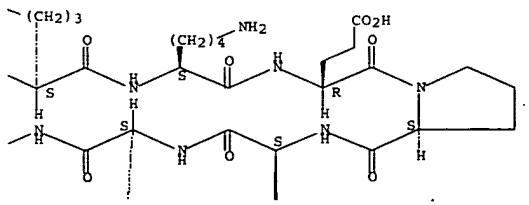
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

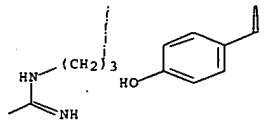


PAGE 1-C



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



RN 664334-40-1 CAPLUS

CN L-Argininamide, N2-(2,4,6-trifluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

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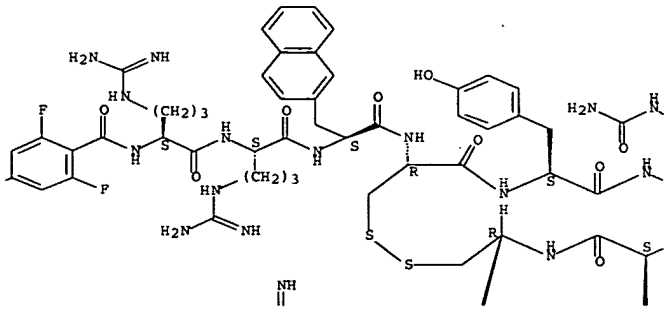
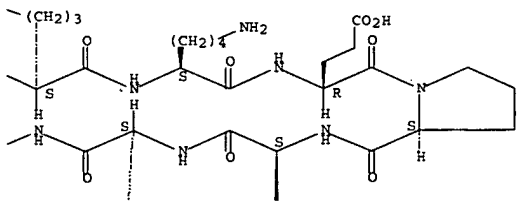
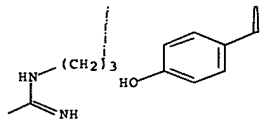


PAGE 1-C



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



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CN L-Argininamide, N2-(4-nitrobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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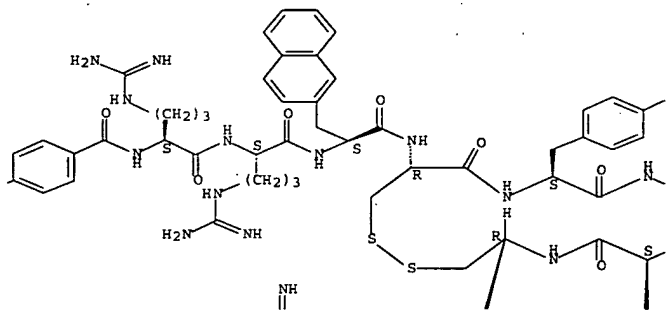
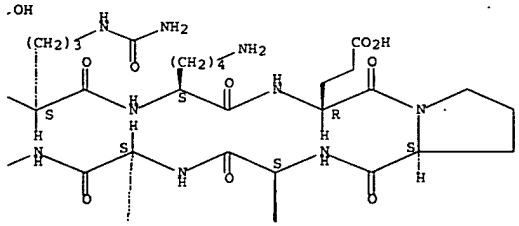
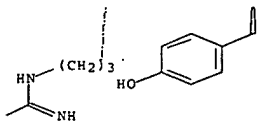


PAGE 1-C



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C

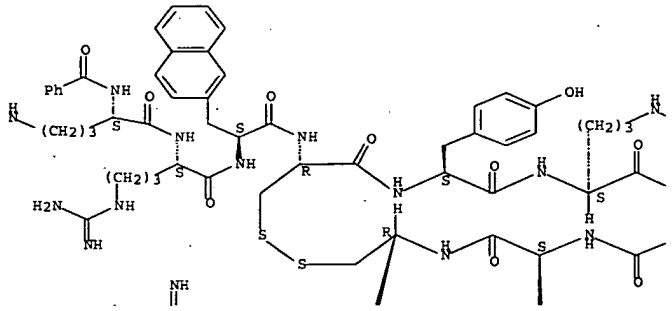


RN 664334-42-3 CAPLUS
CN L-Argininamide, N2-benzoyl-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

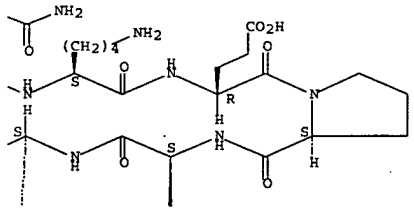
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

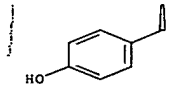


PAGE 1-C



*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

PAGE 2-C



RN 664334-43-4 CAPLUS
CN L-Argininamide, N2-[4-(aminomethyl)benzoyl]-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

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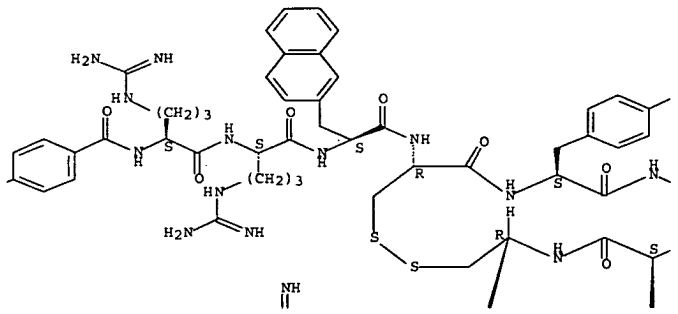
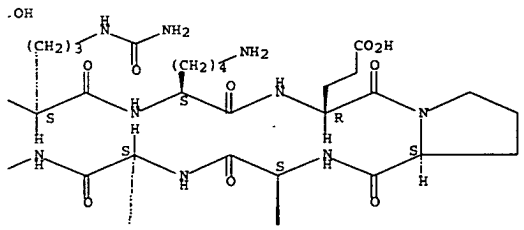
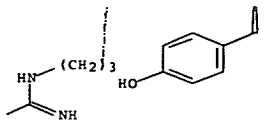


PAGE 1-C



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



RN 664334-44-5 CAPLUS

CN L-Argininamide, N2-(4-aminobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

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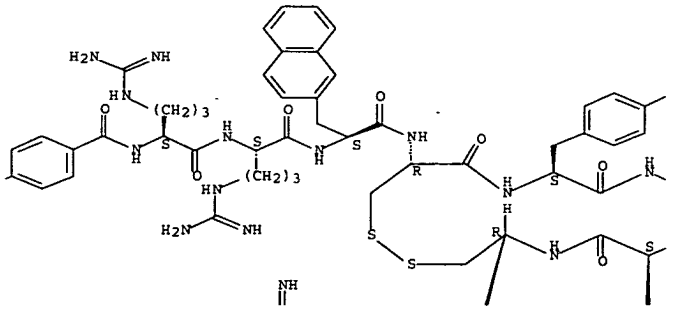
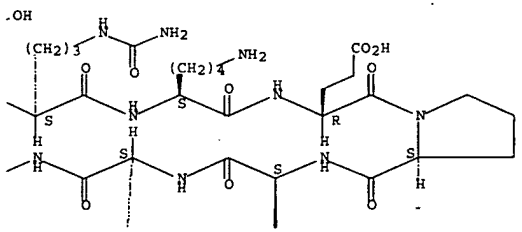
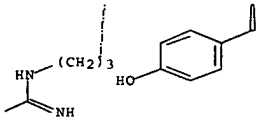


PAGE 1-C



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



RN 664334-45-6 CAPLUS

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Absolute stereochemistry.

PAGE 1-A

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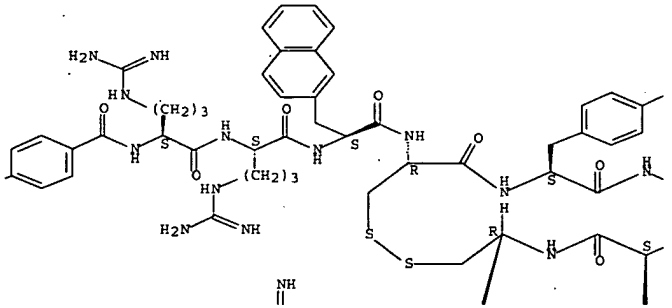
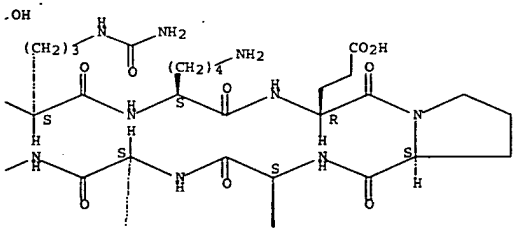
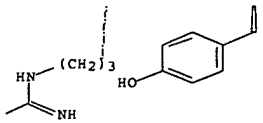


PAGE 1-C



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



RN 664334-46-7 CAPLUS
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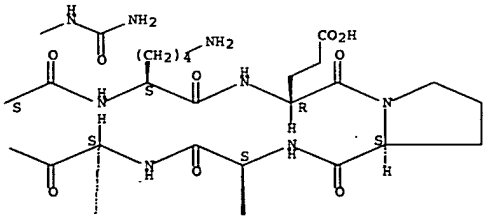
Absolute stereochemistry.

PAGE 1-A

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C



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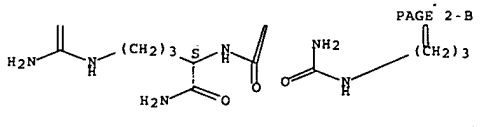
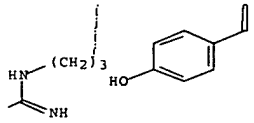


PAGE 2-C



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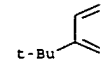
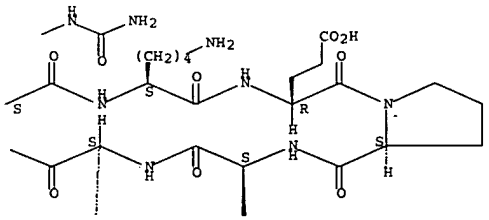
Absolute stereochemistry.

PAGE 1-A

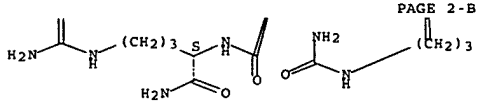


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C



PAGE 2-B



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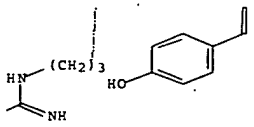

RN 664334-48-9 CAPLUS

CN L-Argininamide, N2-(4-methoxybenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

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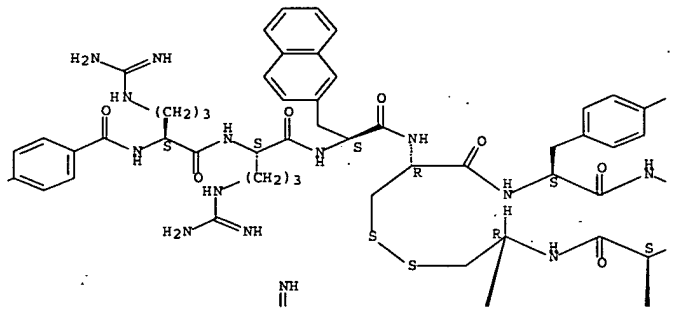
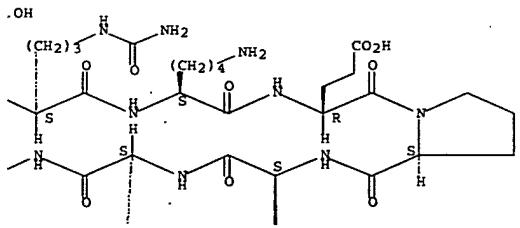
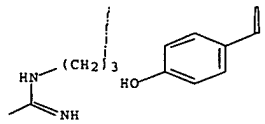


PAGE 1-C



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C

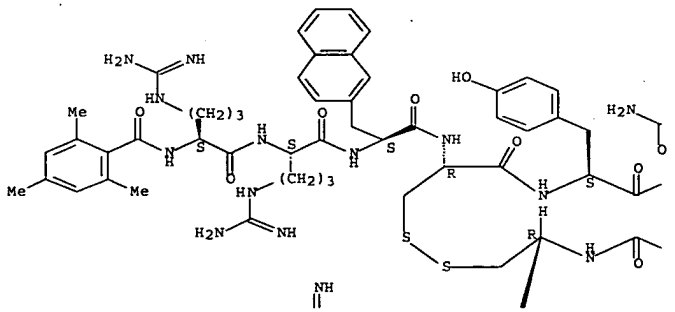


RN 664334-49-0 CAPLUS

CN L-Argininamide, N2-(2,4,6-trimethylbenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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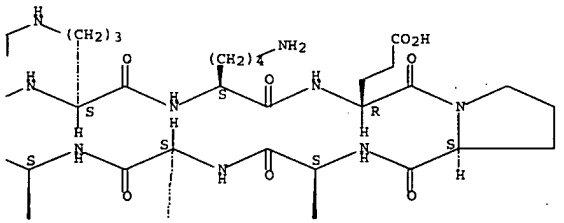

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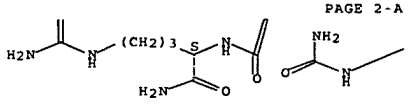

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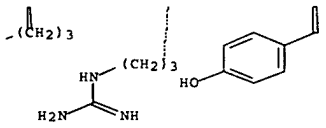


REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:646443 CAPLUS Full-text

DOCUMENT NUMBER: 139:285889

TITLE: T140 analogs as CXCR4 antagonists identified as anti-metastatic agents in the treatment of breast cancer

AUTHOR(S): Tamamura, Hirokazu; Hori, Akira; Kanzaki, Naoyuki; Hiramatsu, Kenichi; Mizumoto, Makiko; Nakashima, Hideki; Yamamoto, Naoki; Otaka, Akira; Fujii, Nobutaka

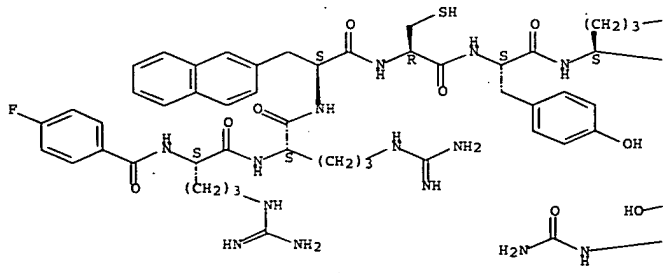
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto, 606-8501, Japan

SOURCE: FEBS Letters (2003), 550(1-3), 79-83

CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Aug 2003
AB A chemokine receptor, CXCR4, and its endogenous ligand, stromal cell-derived factor-1 (SDF-1), have been recognized to be involved in the metastasis of several types of cancers. T140 analogs are peptidic CXCR4 antagonists composed of 14 amino acid residues that were previously developed as anti-HIV agents having inhibitory activity against HIV-entry through its co-receptor, CXCR4. Herein, we report that these compds. effectively inhibited SDF-1-induced migration of human breast cancer cells (MDA-MB-231), human leukemia T cells (Sup-T1) and human umbilical vein endothelial cells at concns. of 10-100 nM in vitro. Furthermore, slow release administration by s.c. injection using an Alzet osmotic pump of a potent and bio-stable T140 analog, 4F-benzoyl-TN14003, gave a partial, but statistically significant (P≤0.05 (t-test)) reduction in pulmonary metastasis of MDA-MB-231 in SCID mice, even though no attempt was made to inhibit other important targets such as CCR7. These results suggest that T140 analogs have potential use for cancer therapy, and that small mol. CXCR4 antagonists could potentially replace neutralizing antibodies as anti-metastatic agents for breast cancer.
IT 608143-91-5
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(T140 analogs as CXCR4 antagonists identified as anti-metastatic agents in treatment of breast cancer)
RN 608143-91-5 CAPLUS
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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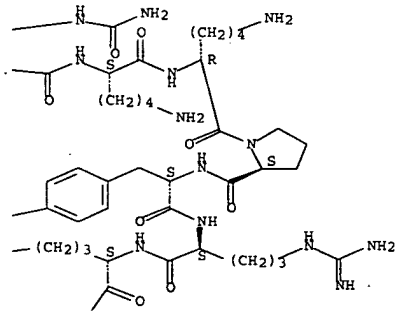

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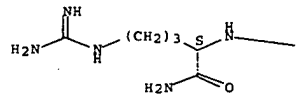

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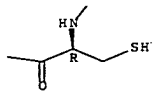


REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

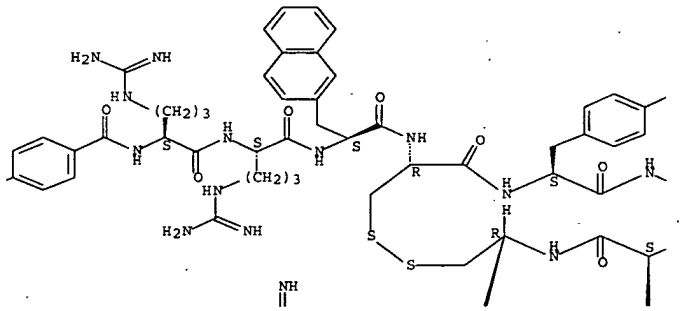
L16 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:449509 CAPLUS Full-text
DOCUMENT NUMBER: 140:212
TITLE: Synthesis of CXCR4 antagonists, T140 derivatives with improved biostability, and their SAR study
AUTHOR(S): Hiramatsu, Kenichi; Tamamura, Hirokazu; Nakashima, Hideki; Otaka, Akira; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Peptide Science (2003), Volume Date 2002, 39th, 213-216

CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Japanese Peptide Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:212
ED Entered STN: 12 Jun 2003
AB T140 is a peptidic CXCR4 antagonist, which selectively inhibits the T-cell line-tropic HIV-1 (X4-HIV-1) infection. Herein, several T140 derivs. such as TE14011, in which basic amino acid residues were substituted by Glu and/or L-citrulline, were found to have strong anti-HIV activity and low cytotoxicity. TE14011 was proven to be stable in mouse serum but unexpectedly unstable in rat liver homogenate. Subsequently, N- and C- terminal modification of TE14011 brought remarkable improvement in anti-HIV activity as well as in biostability.
IT 627872-93-9P 627872-96-2P 627872-97-3P
627872-98-4P 627872-99-5P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and activity of CXCR4 antagonists, T140 derivs. with improved biostability)
RN 627872-93-9 CAPLUS
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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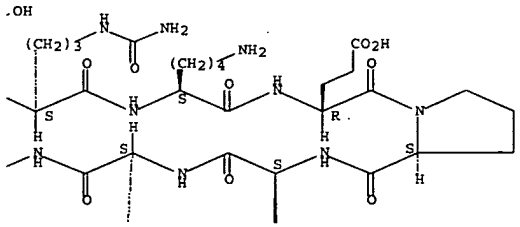
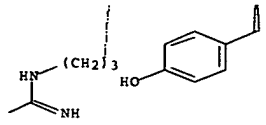


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C

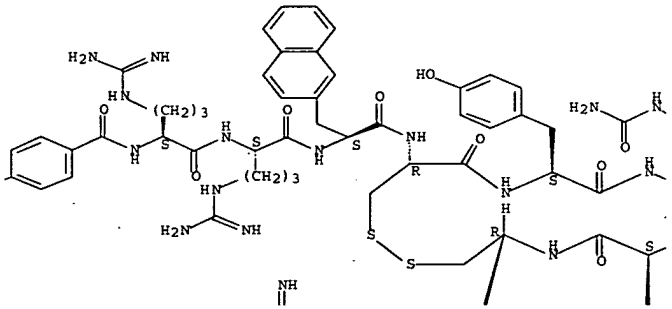


RN 627872-96-2 CAPLUS
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-N-methyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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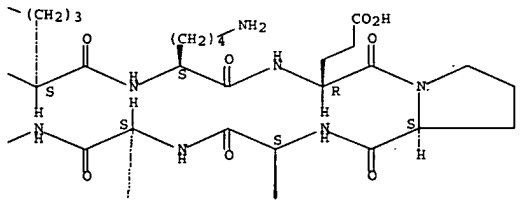
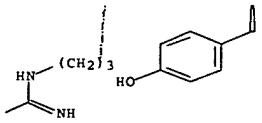


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C

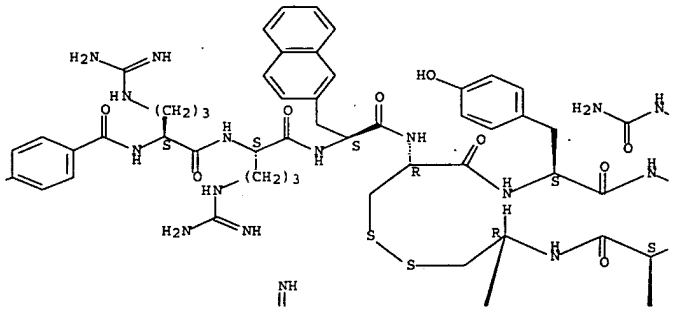


RN 627872-97-3 CAPLUS
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-N-ethyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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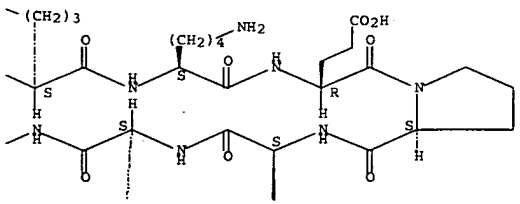
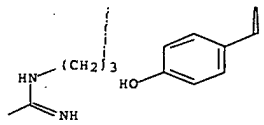


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



RN 627872-98-4 CAPLUS

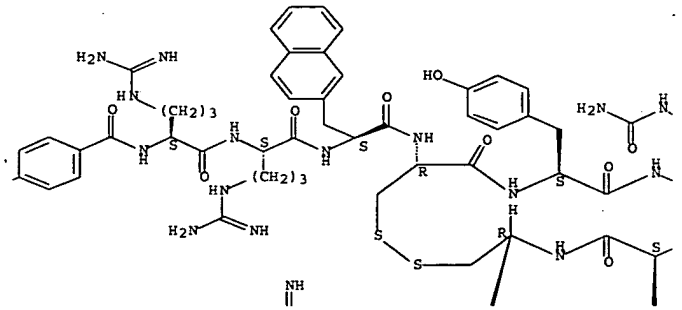
CN L-Argininamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-N-(1-methylethyl)-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

F

PAGE 1-B



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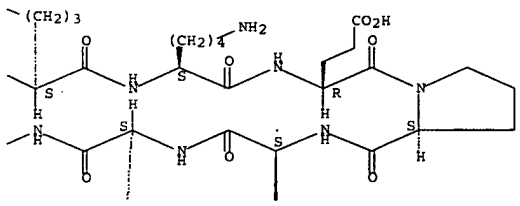
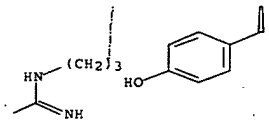


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-C



RN 627872-99-5 CAPLUS

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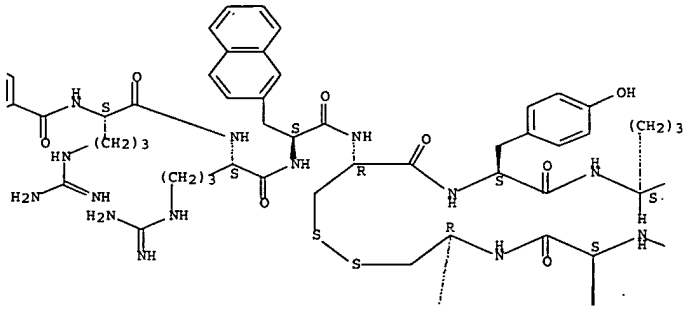
Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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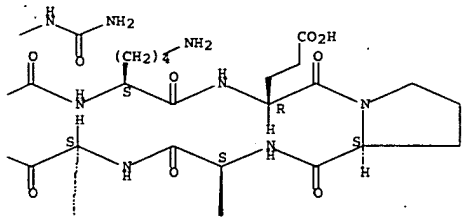

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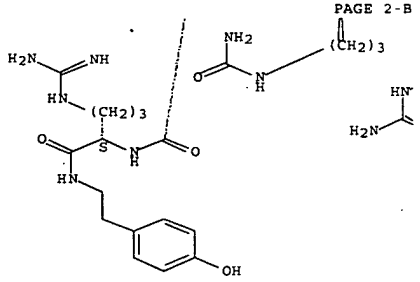

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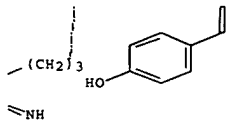


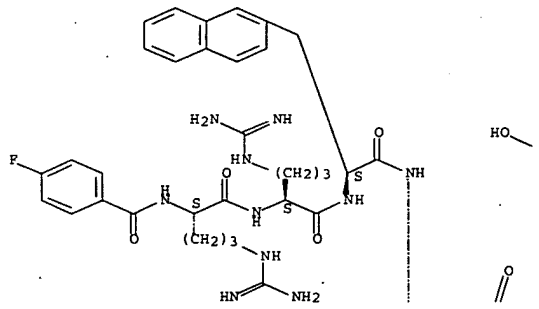
IT 627873-00-1DP, resin-bound 627873-00-1P
627873-01-2DP, resin-bound 627873-01-2P
627873-02-3P 627873-03-4P 627873-04-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and activity of CXCR4 antagonists, T140 derivs. with improved biostability)

RN 627873-00-1 CAPLUS

CN L-Ornithinamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-N5-[[[(2,3-dihydro-2,2,4,6,7-pentamethyl-5-benzofuranyl)sulfonyl]amino]iminomethyl]-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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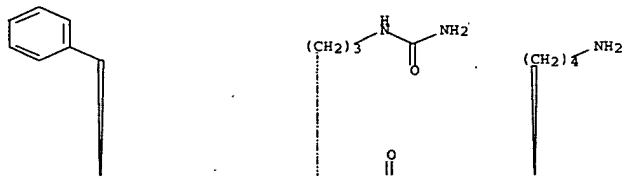

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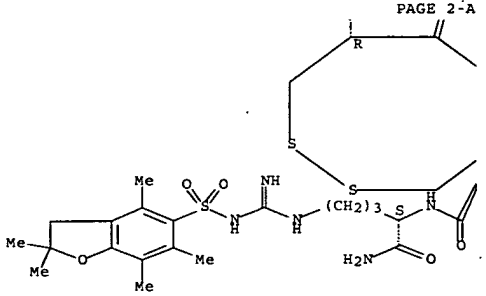
PAGE 2-A



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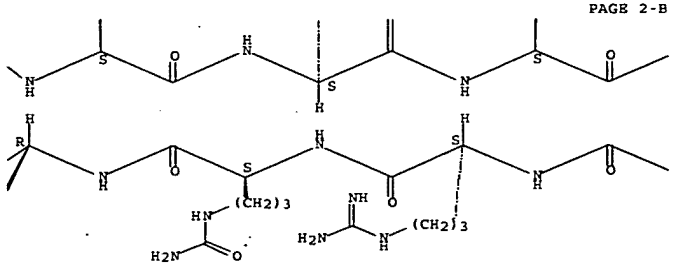

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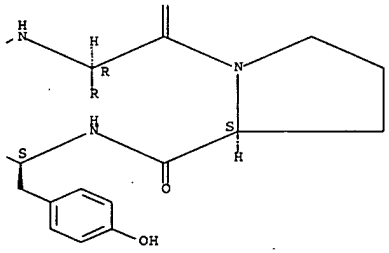

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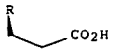
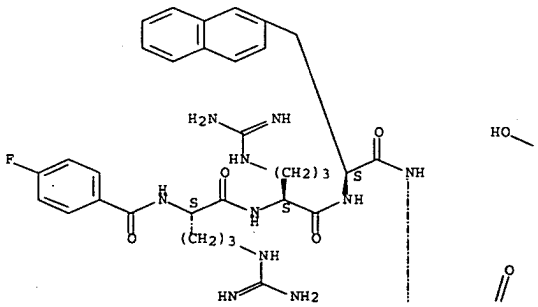


RN 627873-00-1 CAPLUS

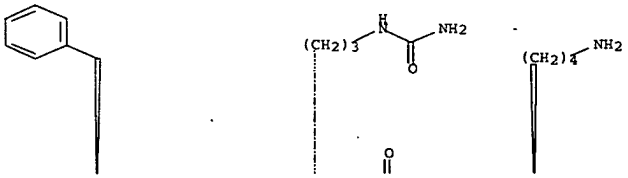
CN L-Ornithinamide, N2-(4-fluorobenzoyl)-L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-α-glutamyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-N5-[[[(2,3-dihydro-2,2,4,6,7-pentamethyl-5-benzofuranyl)sulfonyl]amino]iminomethyl]-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

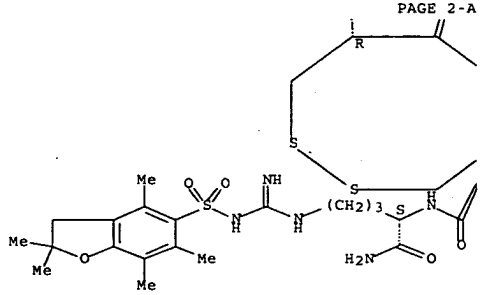


PAGE 1-B



PAGE 1-C

PAGE 2-A



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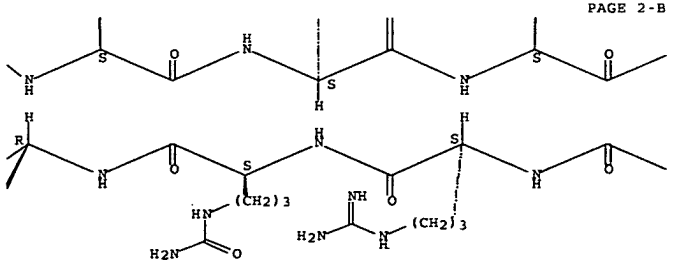
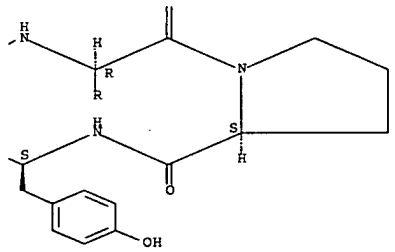


PAGE 2-C



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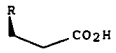

RN 627873-01-2 CAPLUS

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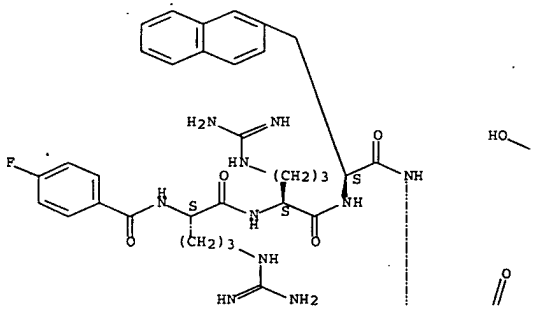
Absolute stereochemistry.

PAGE 1-A



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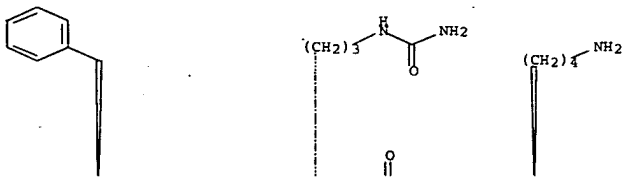

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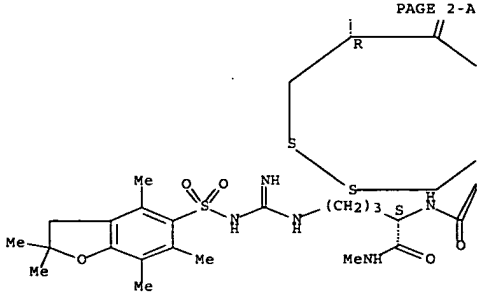

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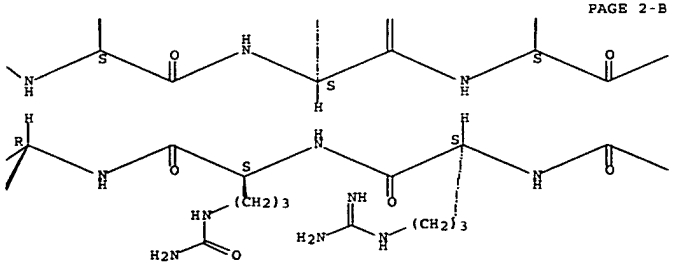

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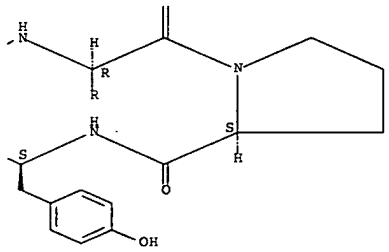

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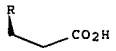

RN 627873-01-2 CAPLUS

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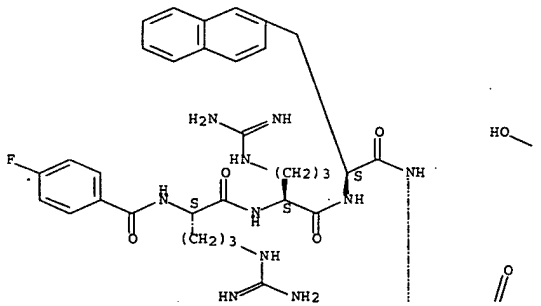
Absolute stereochemistry.

PAGE 1-A



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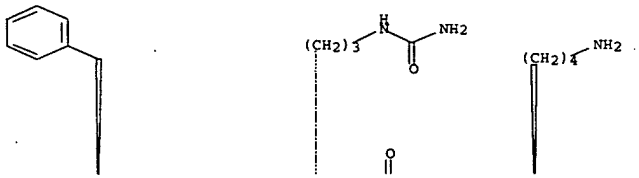

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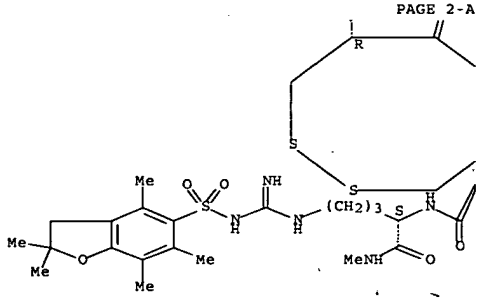

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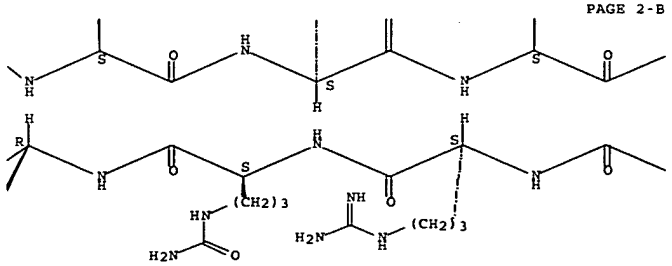

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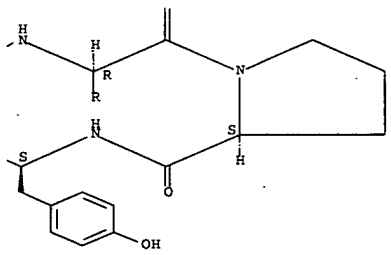

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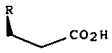

RN 627873-02-3 CAPLUS

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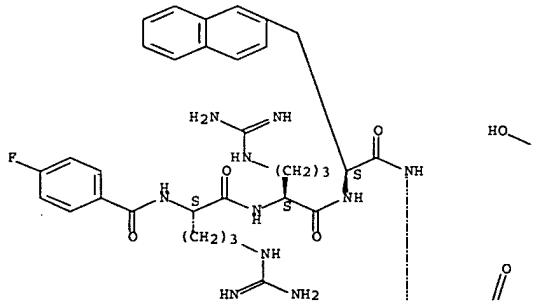
Absolute stereochemistry.

PAGE 1-A



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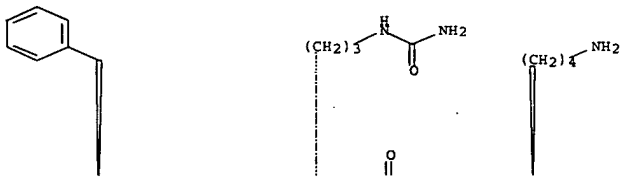

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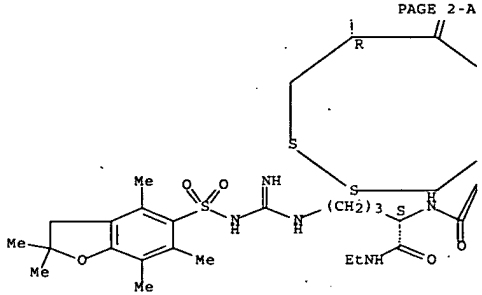

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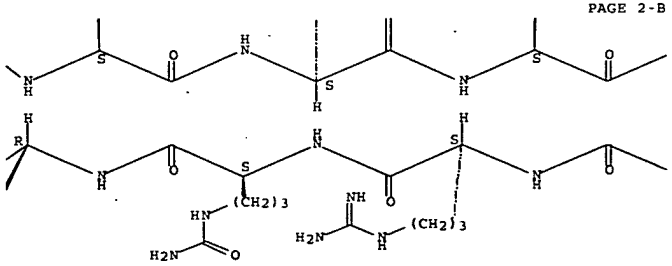

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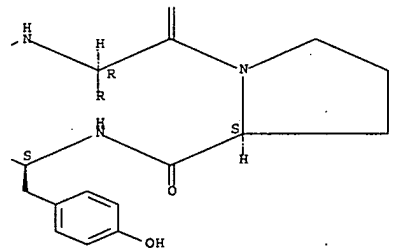

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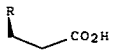

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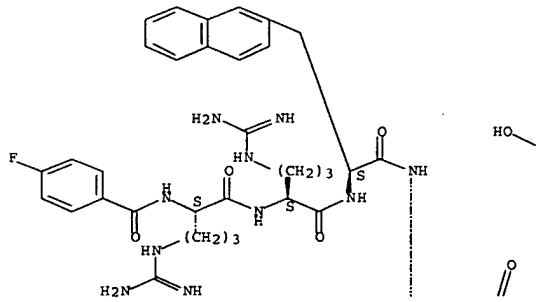
Absolute stereochemistry.

PAGE 1-A



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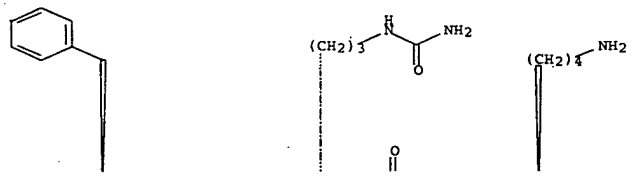

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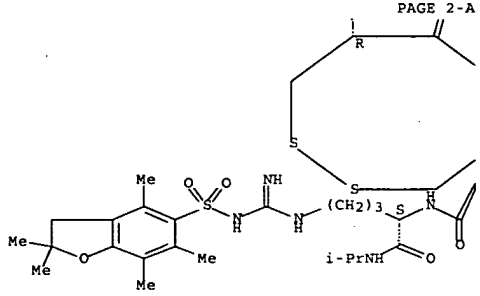

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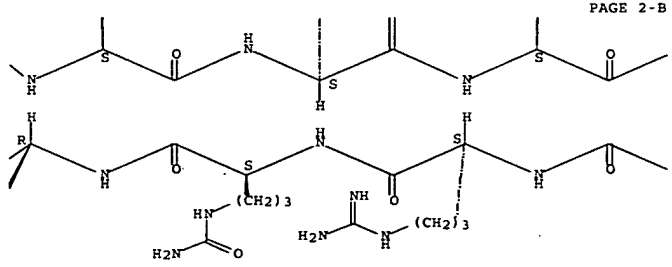

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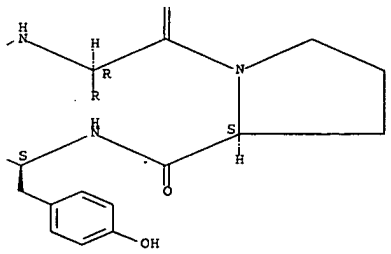

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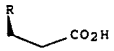

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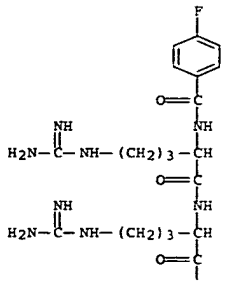

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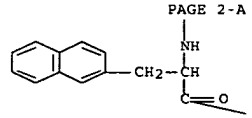

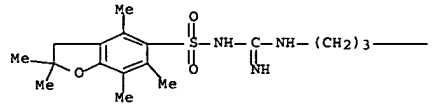

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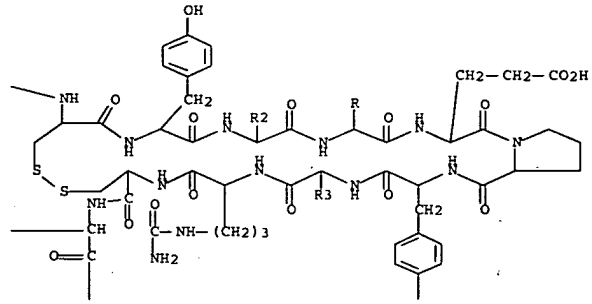

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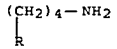

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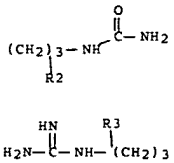

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE COVERS 1980 TO 13 Jun 2007 (20070613/ED)

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L17 ANSWER 1 OF 1 PROUSDDR COPYRIGHT 2007 PROUS SCIENCE on STN
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DOCUMENT NUMBER: 349408
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DRUG NAME: 4F-Benzoyl-TN-14003
CAS REGISTRY NUMBER: 664334-36-5
608143-91-5 (reduced)
MOLECULAR FORMULA: C97 H144 F N33 O19 S2
HIGHEST DEV. PHASE: PRECLINICAL
ORIGINATOR: Takeda
CLASSIFICATION CODE: Oncolytic Drugs
OTHER SOURCE: 385941 (DDR Nonpreferred)
ENTRY DATE: Entered STN: 9 May 2004
Last Updated on STN: 2 Jan 2007

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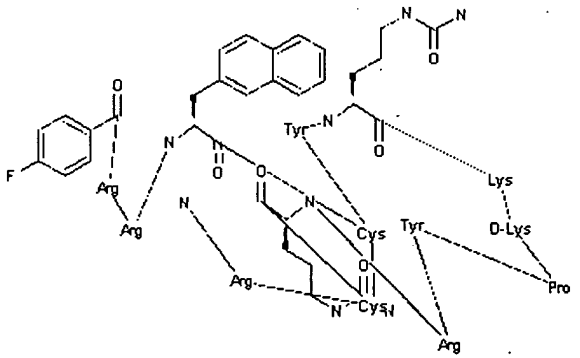

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RefID: 762149 (Text Available)
Drug Data Report, Vol. 25, No. 11, pp 1038, 2003

REFERENCE TEXT: RefID: 762149
ACTION - Chemokine receptor CXCR4 antagonist, a T-140 peptide analogue with potent antimetastatic activity in vitro and in vivo. Compound concentration-dependently (10-100 nM) inhibited SDF-1-induced chemotaxis of human breast cancer MDA-MB-231 cells (by 78% at 100 nM), human leukemia T-cells (SUP-T1) and human umbilical vein endothelial cells (HUVEC). Moreover, in mice bearing MDA-MB-231 tumors, s.c.

administration of compound via an osmotic pump significantly reduced pulmonary metastasis of MDA-MB-231 cells. Potentially useful as an antimetastatic agent.

PATENT REFERENCES:

TITLE: CXCR4 antagonist and use thereof
INVENTOR(S): Fujii, N.; Hori, A.; Tamamura, H.
PATENT ASSIGNEE(S): Takeda
PATENT INFORMATION: EP 1541585 20050615
JP 2004107333 20040408
US 2006264378 20061123
WO 2004020462 20040311
PRIORITY INFORMATION: JP 2002-247843 20020827

TITLE: CXCR4 antagonists for wound healing and re-epithelialization
INVENTOR(S): Fujii, N.; Peled, A.
PATENT ASSIGNEE(S): Hadasit Med. Res. Services Dev.
PATENT ASSIGNEE(S): Kyoto University
PATENT INFORMATION: WO 2006126188 20061130
PRIORITY INFORMATION: US 2005-684160 20050525

REFERENCES:

(1) RefID: 752125, Periodic Publication
"T140 analogs as CXCR4 antagonists identified as anti-metastatic agents in the treatment of breast cancer"
Tamamura, H.; Hori, A.; Kanzaki, N.; et al., FEBS Lett, Vol. 550, No. 1-3, pp 79, 2003

(2) RefID: 822220, Periodic Publication
"Identification of a CXCR4 antagonist, a T140 analog, as an anti-rheumatoid arthritis agent"
Tamamura, H.; Fujisawa, M.; Hiramatsu, K.; Mizumoto, M.; Nakashima, H.; Yamamoto, N.; Otaka, A.; Fujii, N., FEBS Lett, Vol. 569, No. 1-3, pp 99, 2004

(3) RefID: 856844, Congress Literature
"The chemokine receptor CXCR4 as a therapeutic target for several diseases"
Tamamura, H.; et al., Med Chem Symp (23rd Edition), Nov 24 2004-Nov 26 2004, Tsukuba, (Abst 1P-40)

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DICTIONARY FILE UPDATES: 19 JUN 2007 HIGHEST RN 937844-74-1

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http://www.cas.org/support/stngen/stndoc/properties.html

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FILE COVERS 1907 - 20 Jun 2007 VOL 146 ISS 26
FILE LAST UPDATED: 19 Jun 2007 (20070619/ED)

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http://www.cas.org/infopolicy.html
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L13         494 SEA FILE=CAPLUS ABB=ON  HORI A?/AU
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                PRY<2003)


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DOCUMENT NUMBER:          142:309941
TITLE:                    Identification of allosteric peptide agonists of
                          chemokine receptor CXCR4
INVENTOR(S):              Lolis, Elias; Sachpatzidis, Aristidis; Dohlman, Henrik
                          G.; Manfredi, John
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 26 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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     US 2005065064         A1    20050324    US 2003-637911           20030808 <--
PRIORITY APPLN. INFO.:                       US 2002-402474P      P   20020809 <--
ED   Entered STN:  25 Mar 2005
AB   The chemokine receptor CXCR4 is a co-receptor for T-tropic strains of HIV-1.
     A number of small mol. antagonists of CXCR4 are in development, but all are
     likely to lead to adverse effects due to the physiol. function of CXCR4.  To
     prevent these complications, allosteric agonists may be therapeutically useful
     as adjuvant therapy in combination with small mol. antagonists.  A synthetic
     cDNA library coding for 160,000 different SDF-based peptides was screened for
     CXCR4 agonist activity in a yeast strain expressing functional receptor.
     Peptides that activated CXCR4 in an autocrine manner induced colony formation.
     Two peptides, designated RSVM and ASLW, were identified as novel agonists that
     are insensitive to the CXCR4 antagonist AMD3100.  In chemotaxis assays using
     the acute lymphoblastic leukemia cell line CCRF-CEM, RSVM behaves as a partial
     agonist and ASLW as a superagonist.  The superagonist activity of ASLW may be
     related to its inability to induce receptor internalization.  In CCRF-CEM
     cells, the two peptides are also not inhibited by another CXCR4 antagonist,
     T140, or the neutralizing monoclonal antibodies 12G5 and 44717.111.  These
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     results suggest that alternative agonist binding sites are present on CXCR4
     that could be screened to develop mols. for therapeutic use.
IT   229030-20-0, T140
     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
     THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (identification of allosteric peptide agonists of chemokine receptor
        CXCR4)
RN   229030-20-0  CAPLUS
CN   L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-
     tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-
     (aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide
     (CA INDEX NAME)

NTE  modified (modifications unspecified)

SEQ      1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *
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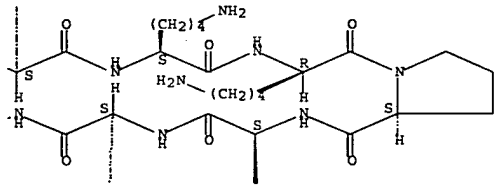

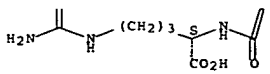

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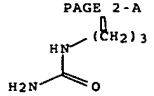

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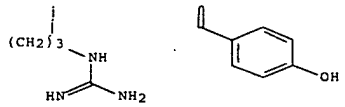


L25 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:198220 CAPLUS Full-text
DOCUMENT NUMBER: 140:247028
TITLE: CXCR4 receptor antagonists for the treatment and prevention of cancer cell metastasis
INVENTOR(S): Burger, Jan Andreas
PATENT ASSIGNEE(S): Universitatsklinikum Freiburg, Germany
SOURCE: Ger. Offen., 13 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10240064	A1	20040311	DE 2002-10240064	20020830 <--
WO 2004024178	A1	20040325	WO 2003-EP9691	20030901 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003255501	A1	20040430	AU 2003-255501	20030901 <--
PRIORITY APPLN. INFO.:			DE 2002-10240064 A	20020830 <--
			WO 2003-EP9691 W	20030901

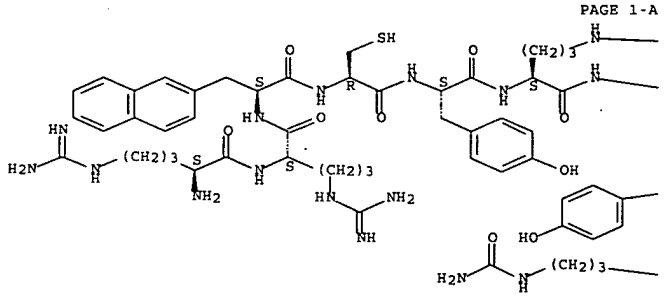
ED Entered STN: 11 Mar 2004
AB The invention discloses the use of a chemokine receptor antagonist as ligand for the CXCR4 receptor for apoptosis-inducing treatment and/or prevention of metastasis of cancer cells in a patient. Antagonists of the invention include e.g. polyphemusin II peptides.
IT 359428-52-7 403620-20-2
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CXCR4 receptor antagonists for treatment and prevention of cancer cell metastasis)
RN 359428-52-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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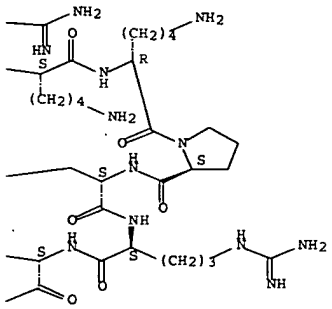

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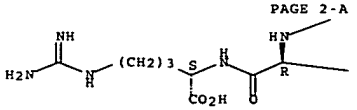


PAGE 2-B

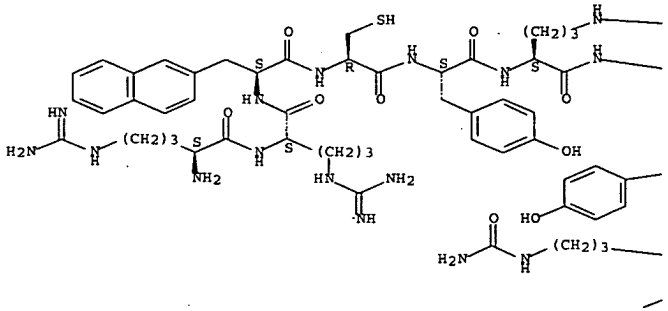
RN 403620-20-2 CAPLUS
CN L-Argininamide, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

NTE modified

SEQ 1 RRACYXKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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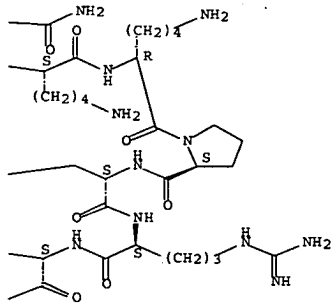

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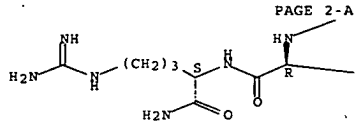

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L25 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:351237 CAPLUS Full-text
DOCUMENT NUMBER: 139:226018
TITLE: Identification of residues in CD4 required for efficient HIV-1 viral entry, and a binding domain for the entry inhibitor T140
AUTHOR(S): Murray, James Lowell
CORPORATE SOURCE: Univ. of Louisville, Louisville, KY, USA
SOURCE: (2002) 92 pp. Avail.: UMI, Order No. DA3062491
From: Diss. Abstr. Int., B 2003, 63(8), 3592
DOCUMENT TYPE: Dissertation
LANGUAGE: English
ED Entered STN: 08 May 2003
AB Unavailable
IT 229030-20-0, T140

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identification of residues in CD4 required for efficient HIV-1 viral entry, and a binding domain for entry inhibitor T140)

RN 229030-20-0 CAPLUS

CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

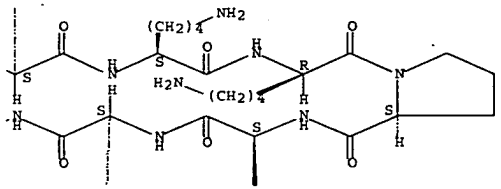
NTE modified (modifications unspecified)

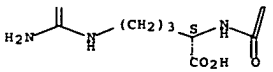
SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B





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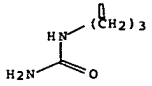

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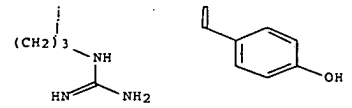

L25 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:908477 CAPLUS Full-text

DOCUMENT NUMBER: 138:378635

TITLE: Env Chimeric virus technology for evaluating human immunodeficiency virus susceptibility to entry inhibitors

AUTHOR(S): Fikkert, Valery; Cherepanov, Peter; Van Laethem, Kristel; Hantson, Anke; Van Remoortel, Barbara; Pannecouque, Christophe; De Clercq, Erik; Debyser, Zeger; Vandamme, Anne-Mieke; Witvrouw, Myriam

CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Louvain, B-3000, Belg.

SOURCE: Antimicrobial Agents and Chemotherapy (2002), 46(12), 3954-3962
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 01 Dec 2002

AB We describe the development of chimeric virus technol. (CVT) for human immunodeficiency virus (HIV) type 1 (HIV-1) env genes gp120, gp41, and gp160 for evaluation of the susceptibilities of HIV to entry inhibitors. This env CVT allows the recombination of env sequences derived from different strains into a proviral wild-type HIV-1 clone (clone NL4.3) from which the corresponding env gene has been deleted. An HIV-1 strain (strain NL4.3) resistant to the fusion inhibitor T20 (strain NL4.3/T20) was selected in vitro in the presence of T20. AMD3100-resistant strain NL3.4 (strain NL4.3/AMD3100) was previously selected by De Vreese et al. NL4.3/AMD3100 contains several mutations in its gp120 gene, whereas NL4.3/T20 has mutations in both gp120 and gp41. Phenotypic anal. revealed that NL4.3/AMD3100 lost its susceptibility to dextran sulfate, AMD3100, AMD2763, T134, and T140 but not its susceptibility to T20, whereas NL4.3/T20 lost its susceptibility only to the inhibitory effect of T20. The recombination of gp120 of NL4.3/AMD3100 and gp41 of NL4.3/T20 or recombination of the gp160 genes of both strains into a wild-type background reproduced the phenotypic (cross-)resistance profiles of the corresponding strains selected in vitro. These data imply that mutations in gp120 alone are sufficient to reproduce the resistance profile of NL4.3/AMD3100. The same can be said for gp41 in relation to NL4.3/T20. In conclusion, we demonstrate the use of env CVT as a research tool in the delineation of the region important for the phenotypic (cross-)resistance of HIV strains to entry inhibitors. In addition, we obtained a proof of principle that env CVT can become a helpful diagnostic tool in assessments of the phenotypic resistance of clin. HIV isolates to HIV entry inhibitors.

IT 205586-56-7, T134 229030-20-0, T140
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(entry inhibitor; env chimeric virus technol. for evaluating human immunodeficiency virus susceptibility to entry inhibitors)

RN 205586-56-7 CAPLUS

CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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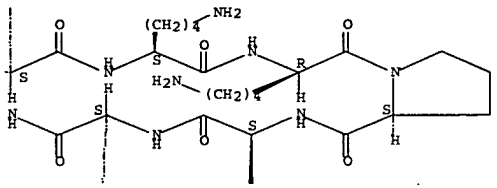

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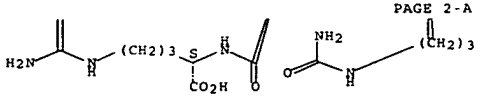

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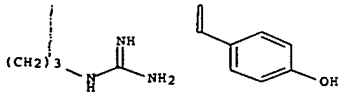


RN 229030-20-0 CAPLUS

CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-

(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

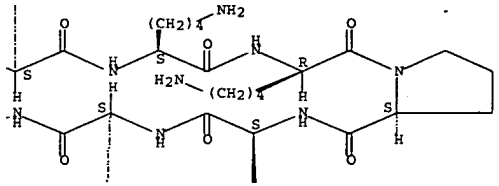
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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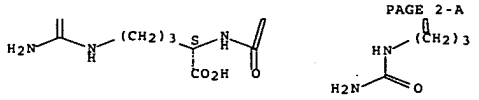

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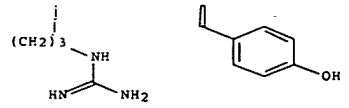


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:537248 CAPLUS Full-text
DOCUMENT NUMBER: 137:123910
TITLE: A point mutation that confers constitutive activity to CXCR4 reveals that T140 is an inverse agonist and that AMD3100 and ALX40-4C are weak partial agonists
AUTHOR(S): Zhang, Wen-Bo; Navenot, Jean-Marc; Haribabu, Bodduluri; Tamamura, Hirokazu; Hiramatu, Kenichi; Omagari, Akane; Pei, Gang; Manfredi, John P.; Fujii, Nobutaka; Broach, James R.; Peiper, Stephen C.
CORPORATE SOURCE: Henry Vogt Cancer Research Institute, University of Louisville, Louisville, KY, 40202, USA
SOURCE: Journal of Biological Chemistry (2002), 277(27), 24515-24521
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Jul 2002
AB CXCR4 is a G protein-coupled receptor for stromal-derived factor 1 (SDF-1) that plays a critical role in leukocyte trafficking, metastasis of mammary carcinoma, and human immunodeficiency virus type-1 infection. To elucidate the mechanism for CXCR4 activation, a constitutively active mutant (CAM) was derived by coupling the receptor to the pheromone response pathway in yeast. Conversion of Asn-119 to Ser or Ala, but not Asp or Lys, conferred autonomous CXCR4 signaling in yeast and mammalian cells. SDF-1 induced signaling in variants with substitution of Asn-119 to Ser, Ala, or Asp, but not Lys. These variants had similar cell surface expression and binding affinity for SDF-1. CXCR4-CAMs were constitutively phosphorylated and present in cytosolic inclusions. Anal. of antagonists revealed that exposure to AMD3100 or ALX40-4C induced G protein activation by CXCR4 wild type, which was greater in the CAM, whereas T140 decreased autonomous signaling. The affinity of AMD3100 and ALX40-4C binding to CAMs was less than to wild type, providing evidence of a conformational shift. These results illustrate the importance of transmembrane helix 3 in CXCR4 signaling. Insight into the mechanism for CXCR4 antagonists will allow for the development of a new generation of agents that lack partial agonist activity that may induce toxicities, as observed for AMD3100.
IT 229030-20-0, t140
RL: BSU (Biological study, unclassified); BIOL (Biological study) (point mutation that confers constitutive activity to CXCR4 reveals that T140 is an inverse agonist and that AMD3100 and ALX40-4C are weak partial agonists)
RN 229030-20-0 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

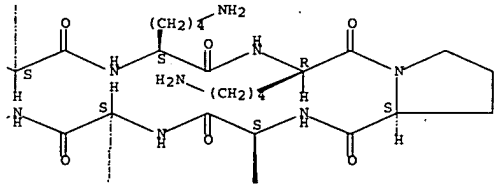
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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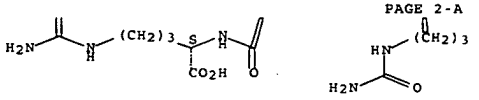

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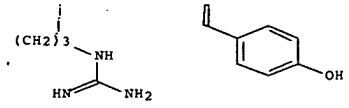


REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:517569 CAPLUS Full-text
DOCUMENT NUMBER: 138:90045
TITLE: Synthesis of novel anti-HIV peptides based on a CXCR4 antagonist, T140, and their SAR study
AUTHOR(S): Hiramatsu, Kenichi; Tamamura, Hirokazu; Omagari, Akane; Nakashima, Hideki; Xu, Younong; Matsuoka, Masao; Otaka, Akira; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Peptide Science (2002), Volume Date 2001, 38th, 175-178
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Japanese Peptide Society

DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 Jul 2002
AB A symposium report. A CXCR4 antagonist, T140, effectively inhibits infection of target cells by T-cell line-tropic strains of HIV-1 (X4-HIV-1). Here, T140 has been proven to be not stable in feline serum due to the cleavage of the C-terminal Arg14 indispensable for anti-HIV activity. On the other hand, the C-terminally amidated analog of T140, TZ14004, has been found to be completely stable in incubation in the serum. The C-terminal amidation is thought to be necessary for stability in serum. In this study, we have conducted a double-L-citrulline (Cit)-scanning study on TZ14004 in due consideration of the total net charges in the whole mol. to find effective CXCR4 inhibitors with increased biostability.
IT 229030-20-0, T140
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation, anti-HIV activity, cytotoxicity and degradation of peptides CXCR4
antagonist and their structure-activity relationship)
RN 229030-20-0 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

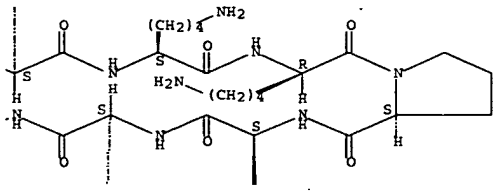
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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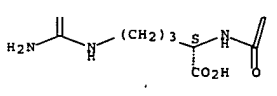

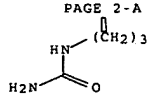

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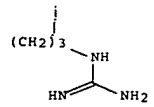
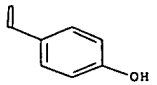




IT 327610-31-1P 359428-59-4P 368874-31-1P
368874-37-7P 368874-38-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, anti-HIV activity, cytotoxicity and degradation of peptides CXCR4
antagonist and their structure-activity relationship)
RN 327610-31-1 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

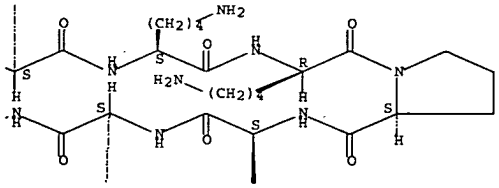
NTE modified (modifications unspecified)

SEQ 1 RRACYXKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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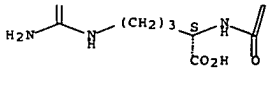

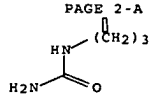

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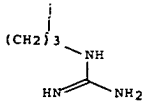
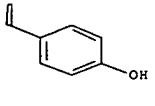




RN 359428-59-4 CAPLUS

CN L-Argininamide, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

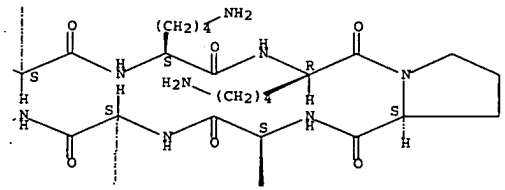
NTE modified

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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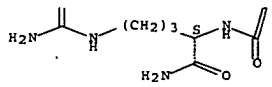

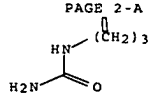

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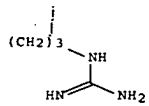
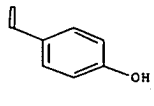




RN 368874-31-1 CAPLUS

CN L-Argininamide, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

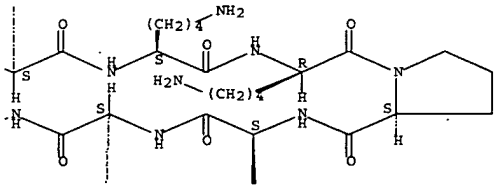
NTE modified

SEQ 1 RRACYXKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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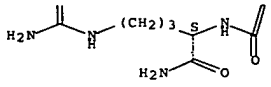

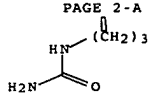

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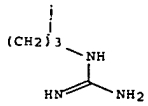

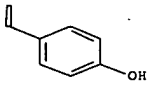

RN 368874-37-7 CAPLUS

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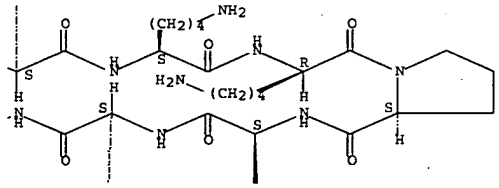
NTE modified (modifications unspecified)

SEQ 1 XRACYXKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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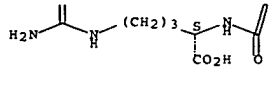

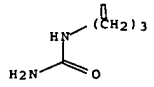

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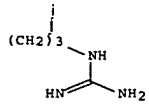
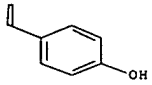




RN 368874-38-8 CAPLUS

CN L-Argininamide, N5-(aminocarbonyl)-L-ornithyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

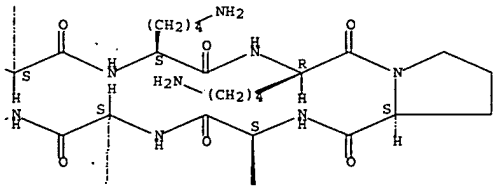
NTE modified

SEQ 1 XRACYXKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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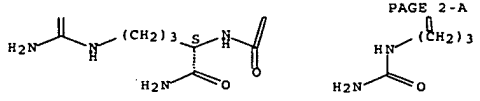

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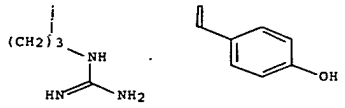


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:416092 CAPLUS Full-text
DOCUMENT NUMBER: 137:153631
TITLE: Stromal cell derived factor 1 synthesis by spleen cells in rodent malaria, and the effects of in vivo supplementation of SDF-1α and CXCR4 receptor blocker
AUTHOR(S): Garnica, Margoth Ramos; Souto, Janeusa Trindade; Silva, Joao Santana; Franco de Andrade, Heitor
CORPORATE SOURCE: Instituto de Medicina Tropical de Sao Paulo, Lab. Protozoologia, Universidade de Sao Paulo, Sao Paulo, 05403-000, Brazil
SOURCE: Immunology Letters (2002), 83(1), 47-53
CODEN: IMLED6; ISSN: 0165-2478

PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 03 Jun 2002
AB The mechanisms of malaria parasite clearance in the host are not well understood, but are ascribed to the intact spleen, the site for parasite clearance. The infection induces a huge increase in spleen volume and cellularity. There is, however, a lack of studies on the splenic production of chemokines, which are small proteins that control homing and activation of immune cells and must be crucial for organized tissue growth. The authors studied the spleen cell production of SDF-1, a primordial chemokine of the CXCL12 class, through mRNA reverse transcriptase and polymerase chain reaction of both isoforms, α and β, in lethal (Plasmodium berghei ANKA) and non-lethal recrudescent malaria (P. chabaudi CR) in BALB/c and C57BL/6 mouse strains. In non-lethal P. chabaudi malaria in C57BL/6 mice, SDF-1α mRNA production clearly peaked before the control of parasitemia, a fact not observed in the same mouse strain infected with lethal P. berghei, when this production was lower and without peaks. The infection of BALB/c mice infected with the same Plasmodium species led to a similar evolution of parasitemia and also chemokine production, albeit at lower levels. SDF-1β synthesis was more constant and regular during both infections, presenting some variation but usually occurring at all the exptl. times. Supplementation of lethal models with SDF-1α i.p., at the time when endogenous stromal cell chemokine production peaked in non-lethal models, induced a clear reduction in parasitemia, probably with prolonged host survival. Blocking SDF-1 action by administration of T-140, a CXCR4 receptor blocker, caused an increase in circulating parasites in the usually benign non-lethal P. chabaudi malaria in C57BL/6 mice, mainly at recrudescence of parasitemia. Thus, SDF-1α production in the spleen plays an important role in rodent malaria, and its supplementation was found to partially correct defects in the control of malaria in lethal models.
IT 229030-20-0, T-140
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stromal cell derived factor 1 (SDF-1) formation by splenocytes in rodent malaria, and effects of in vivo supplementation of SDF-1α and CXCR4 receptor blocker)
RN 229030-20-0 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

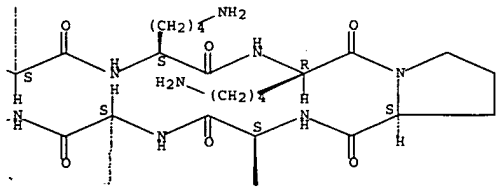
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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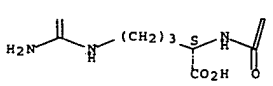

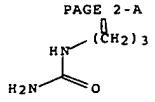

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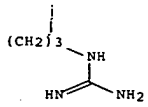
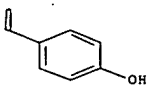




REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:185156 CAPLUS Full-text
DOCUMENT NUMBER: 136:226773
TITLE: Novel polypeptides and anti-HIV drugs containing the same
INVENTOR(S): Fujii, Nobutaka
PATENT ASSIGNEE(S): Seikagaku Corporation, Japan
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020561	A1	20020314	WO 2001-JP7668	20010905 <--
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KR, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PH, PL, RO, SG, SI, SK, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001084419	A5	20020322	AU 2001-84419	20010905 <--
CA 2421183	A1	20030304	CA 2001-2421183	20010905 <--
EP 1323730	A1	20030702	EP 2001-963414	20010905 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004116655	A1	20040617	US 2003-363209	20030305 <--
US 7138488	B2	20061121		
US 2006264605	A1	20061123	US 2006-497225	20060801 <--
PRIORITY APPLN. INFO.:			JP 2000-269296 A	20000905 <--
			JP 2001-92306 A	20010328 <--
			WO 2001-JP7668 W	20010905 <--
			US 2003-363209 A3	20030305

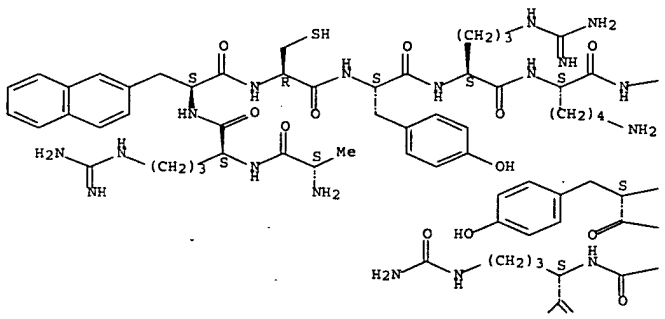
OTHER SOURCE(S): MARPAT 136:226773
ED Entered STN: 15 Mar 2002
AB Polypeptides of A1-Arg-A2-Cys-Tyr-A3-A4-X-A5-A6-Cit Cys-A7 or their salts (wherein A1 is hydrogen or a residue of arginine, lysine, ornithine, citrulline, alanine, or the like; A2 is an aromatic amino acid residue; A3, A4 and A6 are each a residue of arginine, lysine, ornithine, citrulline, or alanine; A5 is a residue of tyrosine, phenylalanine, alanine, naphthylalanine, or citrulline; A7 is a lysine or arginine residue whose carboxyl group may be converted into amido; and X is a residue of D-ornithylproline, prolyl-D-ornithine, D-lysylproline, or the like, with the proviso that any one of A1, A3, A4, A5, A6 and A7 is a residue of alanine or the like or that X is citrulline or the like).
IT 403620-11-1P 403620-12-2P 403620-13-3P
403620-15-5P 403620-18-8P 403620-19-9P
403620-20-2P 403620-21-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel polypeptides and anti-HIV drugs containing the same as protease and reverse transcriptase inhibitors)
RN 403620-11-1 CAPLUS
CN L-Arginine, L-alanyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 ARACYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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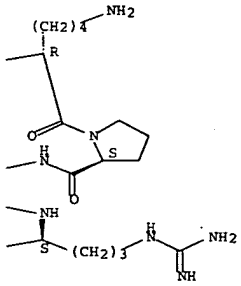

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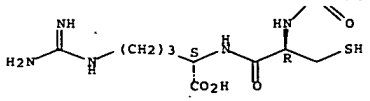


RN 403620-12-2 CAPLUS

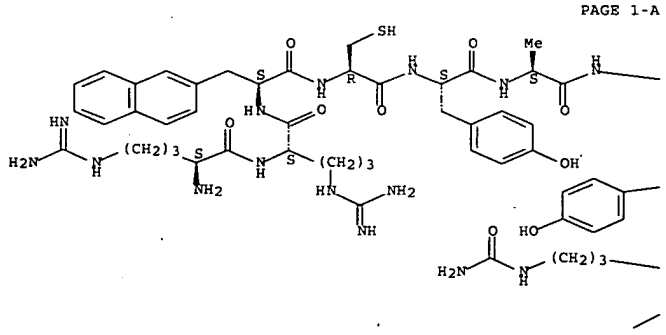
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-alanyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 RRACYAKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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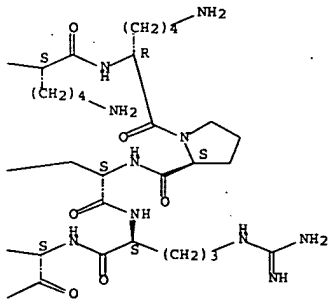

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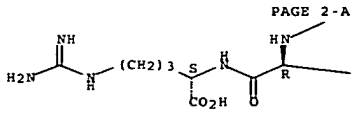

PAGE 2-B

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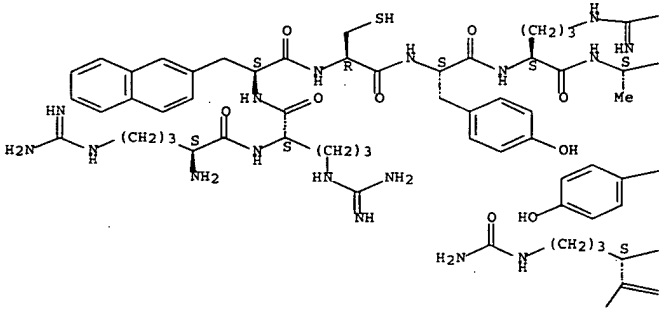
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-alanyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 RRACYRAKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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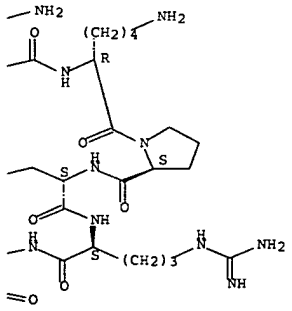

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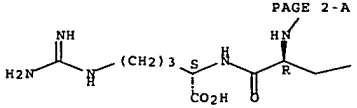


PAGE 2-B

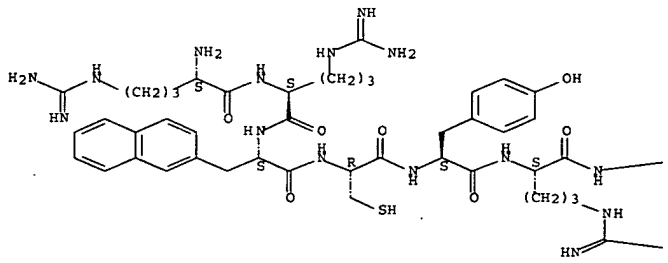
RN 403620-15-5 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-alanyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 RRACYRKKAY RXCR

Absolute stereochemistry.

PAGE 1-A



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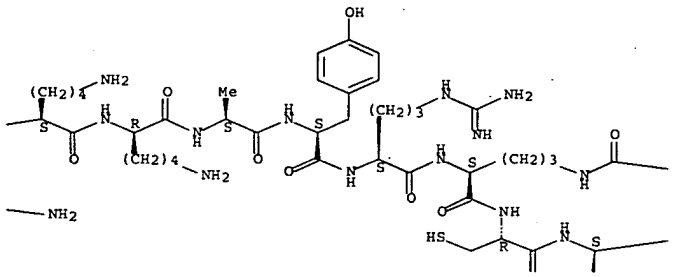

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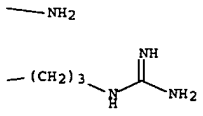

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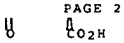

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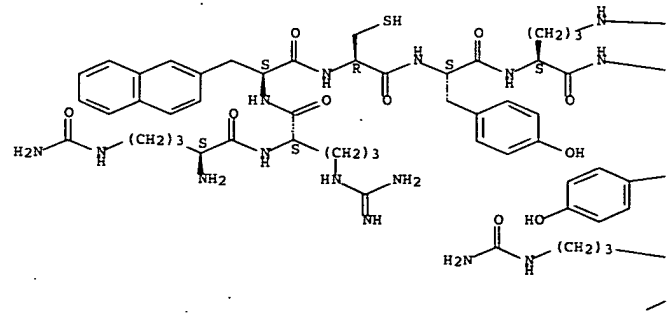
CN L-Arginine, N5-(aminocarbonyl)-L-ornithyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 XRACYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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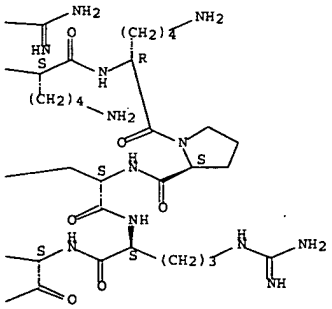

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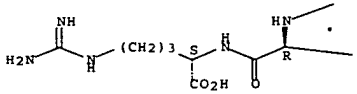


PAGE 2-B

RN 403620-19-9 CAPLUS

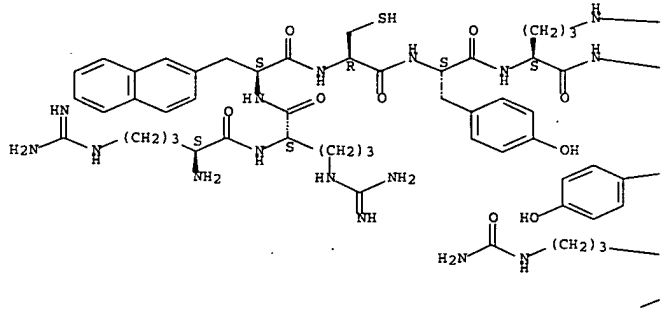
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 RRACYXKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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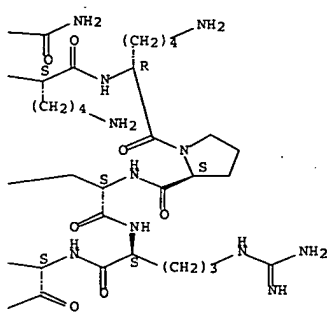

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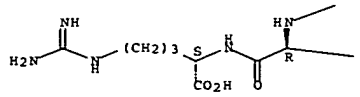

PAGE 2-B

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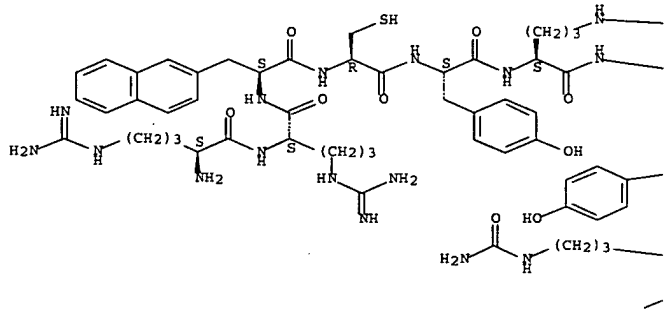
CN L-Argininamide, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

NTE modified

SEQ 1 RRACYXKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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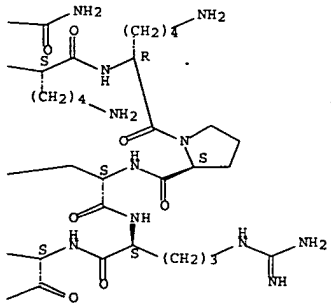

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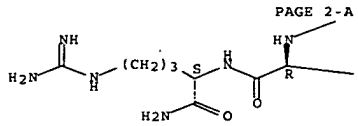

PAGE 2-B

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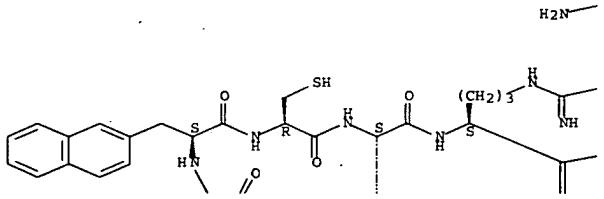
NTE modified (modifications unspecified)

SEQ 1 RRACYRXKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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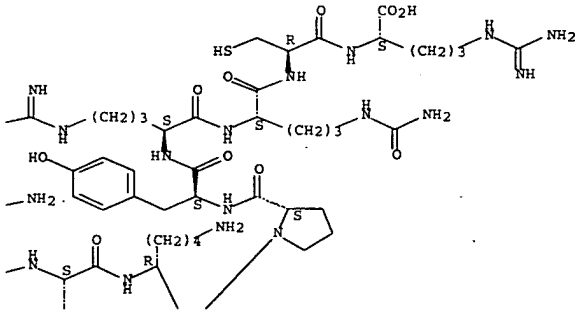

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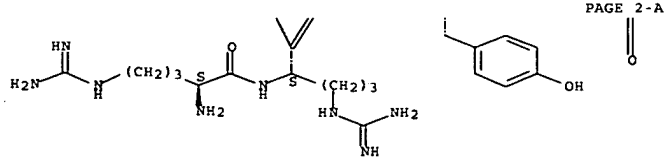

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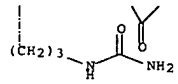


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

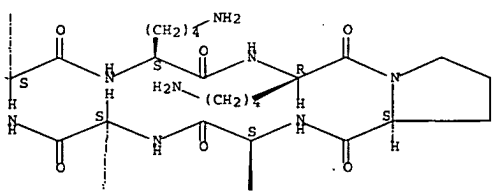
L25 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:175773 CAPLUS Full-text
DOCUMENT NUMBER: 137:155161
TITLE: Synthesis and evaluation of pseudopeptide analogues of a specific CXCR4 inhibitor, T140: The insertion of an (E)-alkene dipeptide isostere into the βII'-turn moiety
AUTHOR(S): Tamamura, Hirokazu; Hiramatsu, Kenichi; Miyamoto, Kazuhide; Omagari, Akane; Oishi, Shinya; Nakashima, Hideki; Yamamoto, Naoki; Kuroda, Yoshihiro; Nakagawa, Terumichi; Otaka, Akira; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(6), 923-928
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:155161
ED Entered STN: 12 Mar 2002
AB A 14-residue peptide, T140, strongly inhibits the T-cell line-tropic HIV-1 (X4-HIV-1) infection, since this peptide functions as a specific antagonist against a chemokine receptor, CXCR4. T140 takes an antiparallel β-sheet structure with a type II' β-turn. In the present paper, we have designed and synthesized several T140 analogs, in which an (E)-alkene dipeptide isostere was inserted into the type II' β-turn moiety, as a bridging study to develop nonpeptidic CXCR4 inhibitors. It has been proven that the turn region of T140 can be replaced by the above surrogate with the maintenance of strong anti-HIV activity.
IT 205586-56-7 359428-58-3 359428-60-7
371916-91-5 445292-10-4 445292-11-5
RL: PAC (Pharmacological activity); BIOL (Biological study)
(evaluation of anti-HIV and cytotoxicity of pseudopeptide analogs of specific CXCR4 inhibitor T140 with insertion of an (E)-alkene dipeptide isostere into the βII'-turn moiety)
RN 205586-56-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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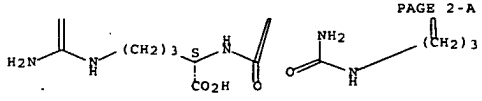

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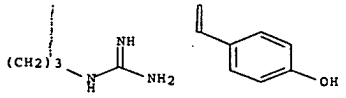

RN 359428-58-3 CAPLUS

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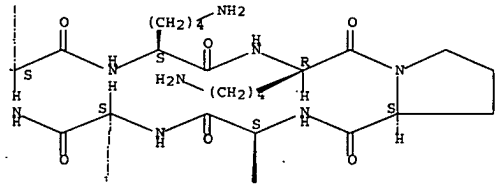
NTE modified

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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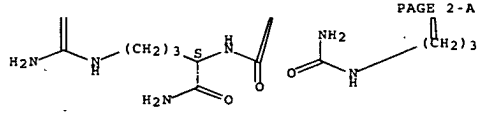

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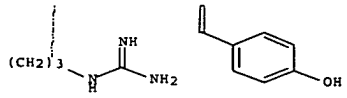

RN 359428-60-7 CAPLUS

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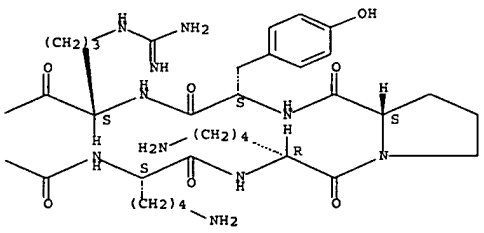
NTE modified

SEQ 1 RRCCYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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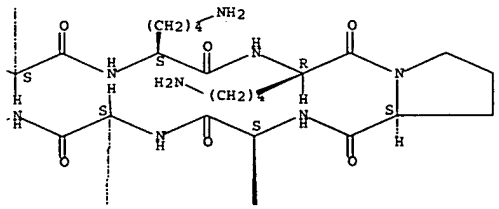
NTE modified

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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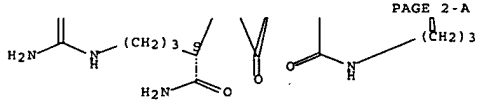

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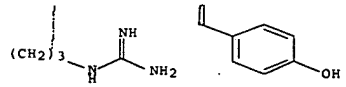

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CN L-Arginine, L-arginyl-L-arginyl-3-(1-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

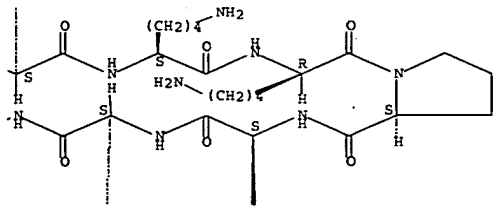
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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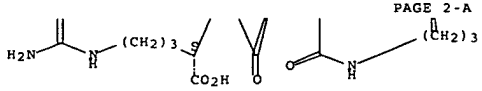

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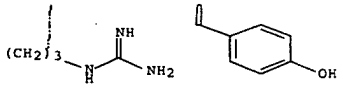

RN 445292-11-5 CAPLUS
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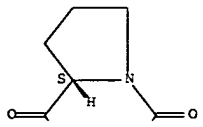
NTE modified

SEQ 1 RRCCYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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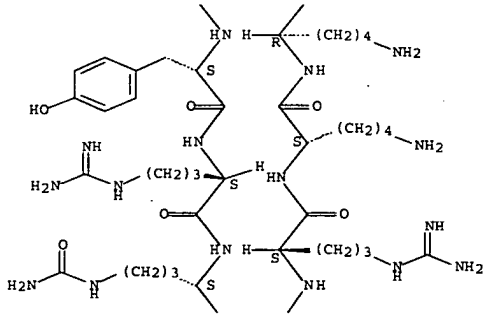

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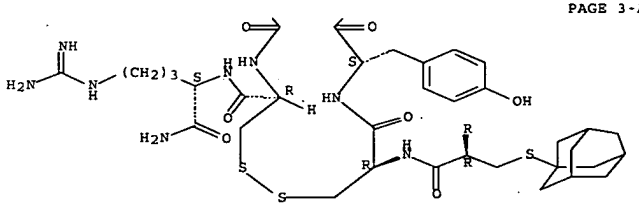

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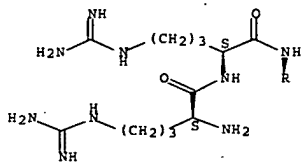


REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:170722 CAPLUS Full-text
DOCUMENT NUMBER: 137:179373

TITLE: Certification of the Critical Importance of 1-3-(2-Naphthyl)alanine at Position 3 of a Specific CXCR4 Inhibitor, T140, Leads to an Exploratory Performance of Its Downsizing Study

AUTHOR(S): Tamamura, Hirokazu; Omagari, Akane; Hiramatsu, Kenichi; Oishi, Shinya; Habashita, Hiromu; Kanamoto, Taisei; Gotoh, Kazuyo; Yamamoto, Naoki; Nakashima, Hideki; Otaka, Akira; Fujii, Nobutaka

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto, 606-8501, Japan

SOURCE: Bioorganic & Medicinal Chemistry (2002), 10(5), 1417-1426
CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 08 Mar 2002

AB We have previously found that a 14-amino acid residue-peptide, T140, inhibits infection of target cells by T cell line-tropic HIV-1 (X4-HIV-1) through its specific binding to a chemokine receptor, CXCR4. Here, the importance of an 1-3-(2-naphthyl)alanine (Nal) residue at position 3 in T140 for high anti-HIV activity and inhibitory activity against Ca2+ mobilization induced by stromal cell-derived factor (SDF)-1α- stimulation through CXCR4 has initially been shown by the synthesis and biol. evaluation of several analogs, where Nal3 is substituted by diverse aromatic amino acids. Next, the order of the N-terminal 3 residues (Arg1-Arg2-Nal3) has been proved to be important from the structure-activity relationship (SAR) study shuffling these residues. Based on these results, we have found 10-residue peptides possessing modest anti-HIV activity by systematic antiviral evaluation of a series of synthetic, shortened analogs of T140.

IT 452058-04-7P 452058-06-9P 452058-08-1P
452058-10-5P 452058-12-7P 452058-13-8P
452058-14-9P 452058-15-0P 452058-18-3P
452058-19-4P 452058-21-8P 452058-22-9P
452058-23-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(structure-activity relationship study on synthetic and shortened analogs of CXCR4 inhibitor, T140 as antiHIV agents)

RN 452058-04-7 CAPLUS

CN L-Arginine, L-phenylalanyl-L-arginyl-L-arginyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

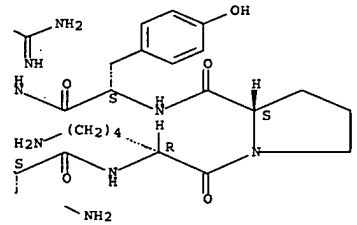
SEQ 1 FRRCYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C



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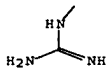

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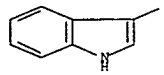
SEQ 1 WRRCYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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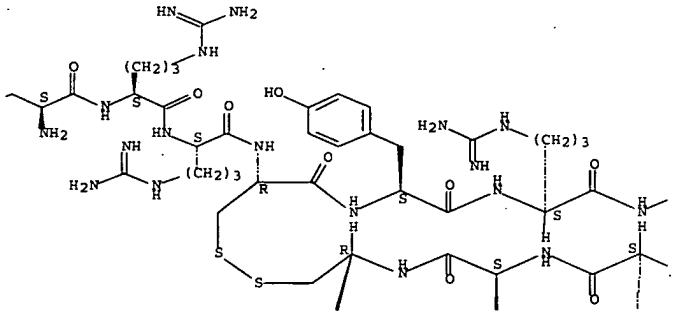

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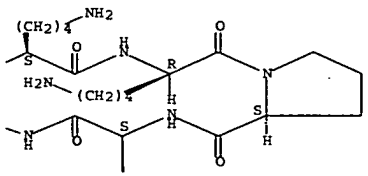

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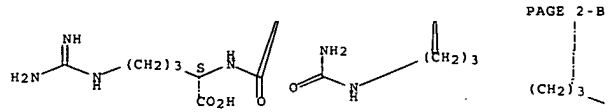

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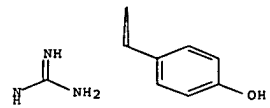

RN 452058-08-1 CAPLUS

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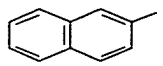
NTE modified (modifications unspecified)

SEQ 1 ARRCYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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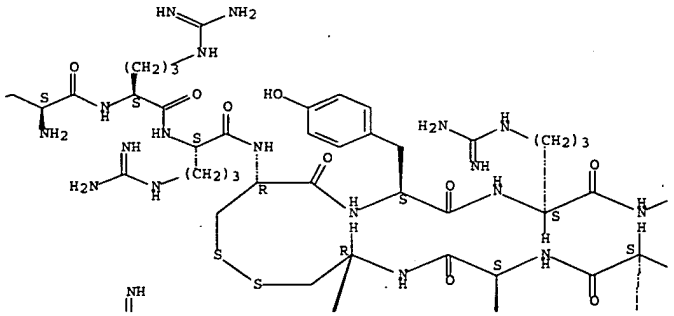

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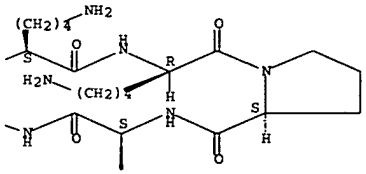

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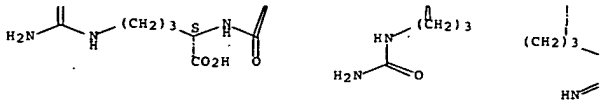

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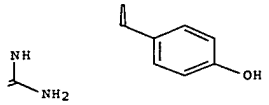

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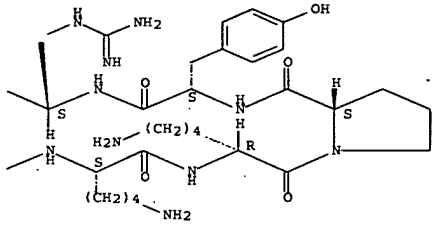
NTE modified (modifications unspecified)

SEQ 1 RRCYRKKPYR XCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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SEQ 1 RFRCYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A

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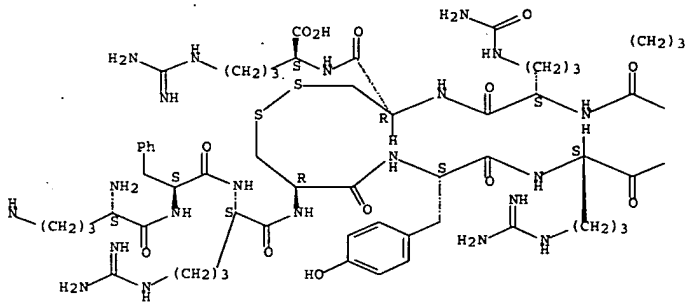

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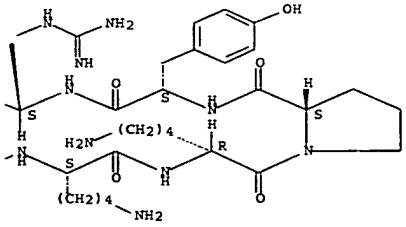

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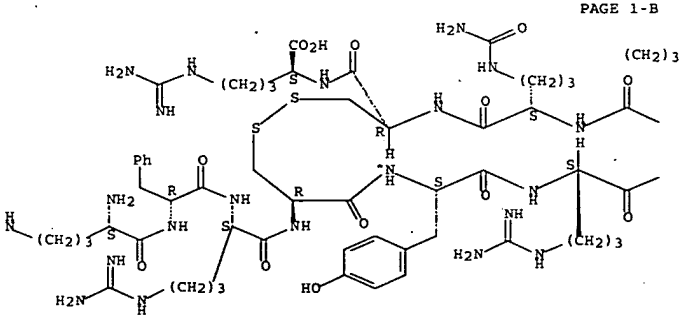
SEQ 1 RFRCYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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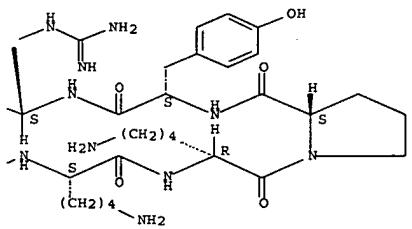

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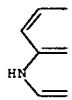
SEQ 1 RWRCYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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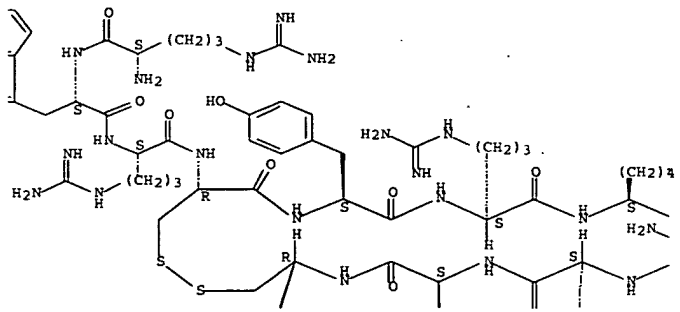

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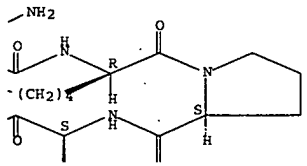

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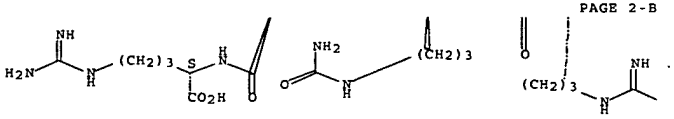

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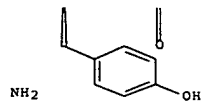

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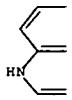
SEQ 1 RWRCYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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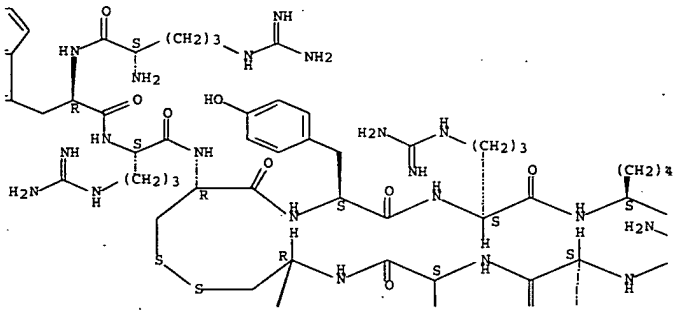

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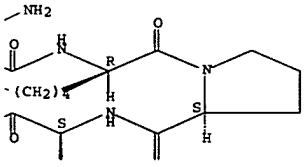

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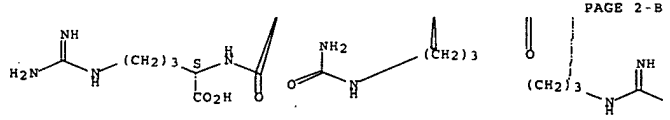

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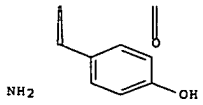

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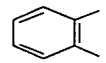
NTE modified (modifications unspecified)

SEQ 1 RARCYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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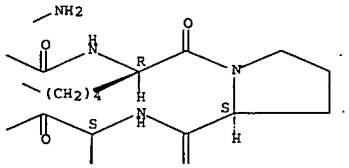

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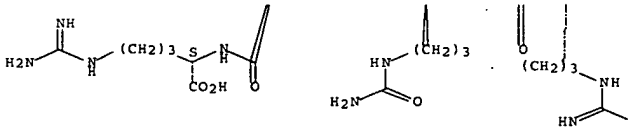

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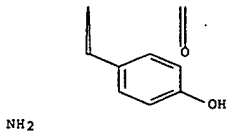

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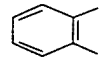
NTE modified (modifications unspecified)

SEQ 1 RARCYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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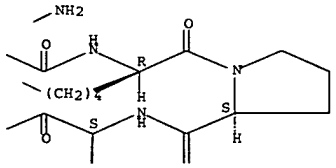

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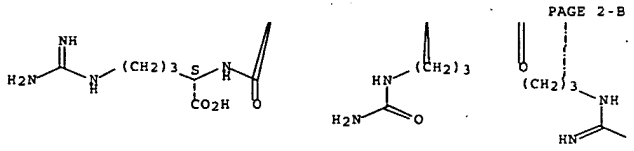

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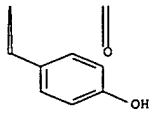

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NTE modified (modifications unspecified)

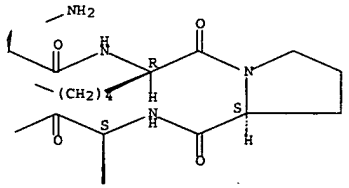
SEQ 1 RACYRKKPYR XCR

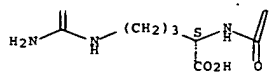
Absolute stereochemistry.

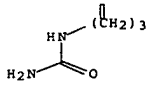
PAGE 1-A

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C







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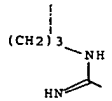

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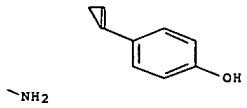

RN 452058-22-9 CAPLUS
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NTE modified (modifications unspecified)

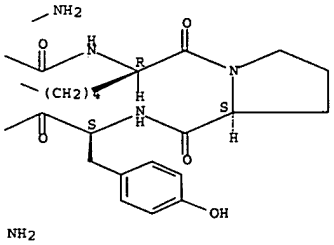
SEQ 1 ACYRKKPYRX CR

Absolute stereochemistry.

PAGE 1-A

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-C



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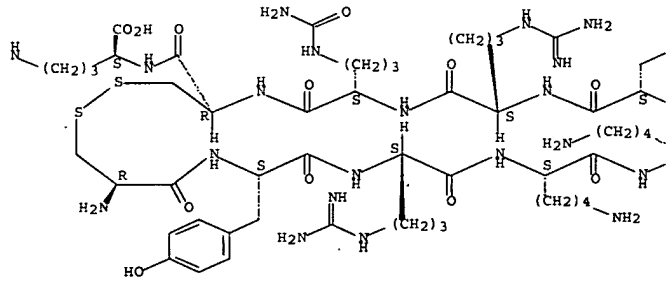
SEQ 1 CYRKKPYRXC R

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



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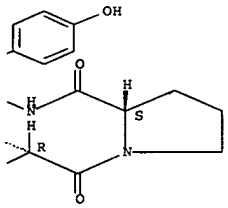


REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:813757 CAPLUS Full-text
DOCUMENT NUMBER: 136:112068
TITLE: Development of selective antagonists against an HIV second receptor
AUTHOR(S): Tamamura, Hirokazu
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku, Kyoto, 606-8501, Japan
SOURCE: Yakugaku Zasshi (2001), 121(11), 781-792
CODEN: YKKZAJ; ISSN: 0031-6903
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
ED Entered STN: 09 Nov 2001
AB A review. The authors have discovered a highly selective CXCR4 antagonist, T22 ([Tyr5,12, Lys7]-polyphemusin II), and its shortened potent analogs, T140 and TC14012, which strongly inhibit the T-cell line-tropic HIV-1 (X4-HIV-1) infection through their specific binding to a chemokine receptor, CXCR4. CXCR4 is a major coreceptor (second receptor) for the entry of X4 HIV-1 into

T-cells. These peptides have been found through the structure-activity relationship (SAR) study on tachyplesins and polyphemusins, which function as self-defense peptides of horseshoe crabs with immature immune systems. T140 and TC14012 showed the highest level of anti-HIV activity and antagonism of target cell entry by X4-HIV-1 among all the CXCR4 antagonists that have been reported to date. Addnl., bifunctional anti-HIV agents based on the specific CXCR4 antagonists (T140 analogs)-3'-azido-3'-deoxythymidine (AZT) conjugation have been synthesized and evaluated, since T140 analogs can possibly work as a carrier of AZT targeting T-cells due to their specific affinity for CXCR4 on T cells. T22 have two disulfide bonds and a Trp residue in the mol. In connection with this study, novel facile and side-reaction-free methodologies for disulfide bond formation have been established for the increase of the efficiency of SAR studies. Furthermore, the completely stereocontrolled synthetic process for a couple of (E)-alkene dipeptide isosteres starting from L-amino acid has been established in order to facilitate nonpeptidylation studies on peptide-lead candidates. In this review, the authors wish to summarize our recent research on the development of specific antagonists against the HIV second receptor CXCR4, involving studies on the establishment of efficient methodologies for the facile synthesis of peptides and peptide mimetics.

IT 229030-20-0, T140
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(development of selective antagonists against an HIV second receptor)

RN 229030-20-0 CAPLUS

CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

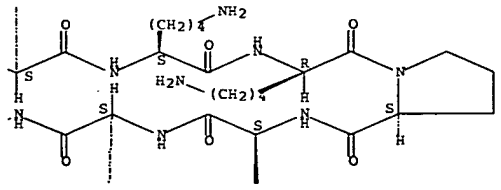
NTE modified (modifications unspecified)

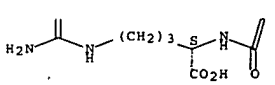
SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B





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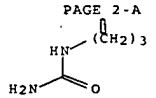

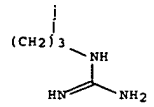

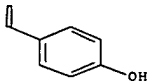

PAGE 2-B

L25 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:661457 CAPLUS Full-text
DOCUMENT NUMBER: 135:227249
TITLE: Preparation of alkane- or alkene-bridged cyclopeptides and peptide cyclic disulfides as antiviral agents
INVENTOR(S): Fujii, Nobutaka; Nakashima, Hideki
PATENT ASSIGNEE(S): Japan
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064716	A1	20010907	WO 2001-JP1642	20010302 <--

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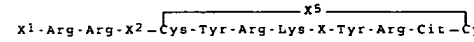
PRIORITY APPLN. INFO.: JP 2000-59495 A 20000303 <--
OTHER SOURCE(S): MARPAT 135:227249
ED Entered STN: 10 Sep 2001
GI



AB Novel antiviral compds. represented by the general formula [I; X = Y1-X3-Y2; X1 = NH2, NH:C(NMe2)2; X2 = amino acid having an aromatic ring; X3 = a single bond, CR1:CH (wherein R1 = H, C1-5 alkyl, halo); X4 = NHR2 (wherein R2 = H, C1-5 alkyl), OH; X5 = CH2-S-S-CH2, C4-8 alkylene, C4-8 alkenylene; Y1 = Arg, Lys, Orn, other basic L- or D-amino acids; Y2 = Pro, Ala, Val, other aliphatic L- or D-amino acid; Cit = citrulline; provided that the compds. where (1) X1 = NH2, X2 = NaI, X = D-Lys-Pro, X4 = OH, and X5 = CH2-S-S-CH2 and (2) X1 = NH2, X2 = Trp, X = D-Lys-Pro, X4 = OH, and X5 = CH2-S-S-CH2 are excluded.] or pharmaceutically acceptable salts thereof are prepared Anti-HIV agents containing the same as the active ingredient are also claimed. These peptide compds. are antagonists of glycoproteins, in particular CXCR4 chemokine receptors, and have an excellent antiviral activity, the stability of which is improved in vivo. Thus, ring-closing metathesis (RCM) of Fmoc-Arg(Pmc)-Arg(Pmc)-Nal-Hag-Tyr(t-Bu)-Arg(Pmc)- Lys(Boc)-D-Lys(Boc)-Tyr(t-Bu)-Arg(Pmc)-Cit-Hag-Arg(Pmc)-4-alkoxybenzyl alc.-PEG-resin [wherein Pmc = 2,2,5,7,8-pentamethylchroman-6-sulfonyl, Nal = 3-(2-naphthyl)alanine residue, Hag = L-homoallylglycine residue, Cit = citrulline] using Grubbs' ruthenium catalyst in CH2Cl2 under refluxing for 12 h followed by deprotection and resin cleavage gave I [X1 = H2N, X2 = 3-(2-naphthyl)alanine residue, X3 = a single bond, Y1 = D-Lys, Y2 = Pro, X4 = OH, X5 = (E)- and (Z)-CH2CH:CHCH2] which was hydrogenated over Pd-Al2O3 to give I (X5 = (CH2)4; X1, X2, X3, Y1, Y2, X4 = same as above) (II). II in vitro inhibited the human stromal cell-derived factor (SDF)-induced increase in cellular Ca ion concentration in CHO (Chinese hamster ovarian) cells over-expressing CXCR4 chemokine receptor with IC50 of 0.3-1 nM (CXCR4/SDF).

IT 205586-56-7P 229030-20-0P 359428-39-0P
359428-50-5P 359428-58-3P 359428-59-4P
359428-60-7P 359428-61-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclopeptides and peptide cyclic disulfides as antagonists of CXCR-4 chemokine receptors and antiviral agents, in particular against HIV)

RN 205586-56-7 CAPLUS

CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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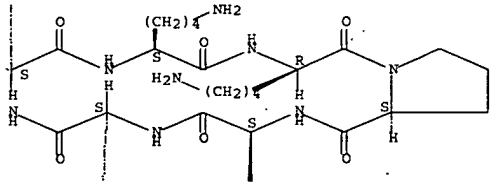

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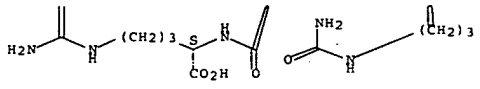

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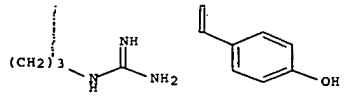

RN 229030-20-0 CAPLUS

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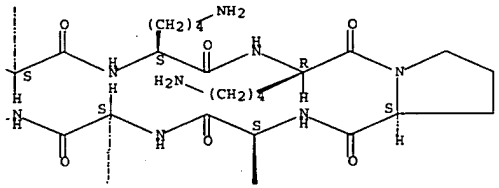
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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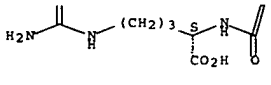

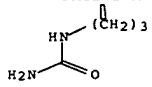

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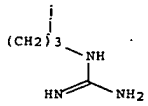

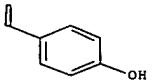

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NTE modified

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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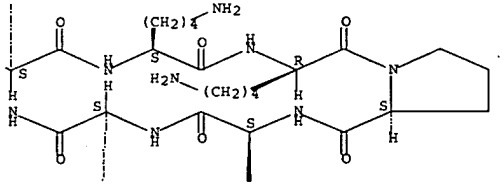

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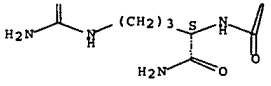

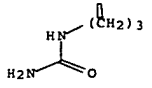

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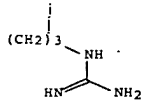

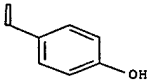

RN 359428-50-5 CAPLUS

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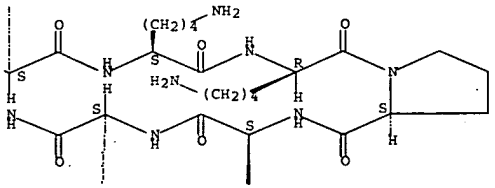
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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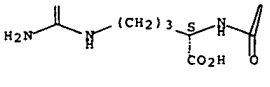

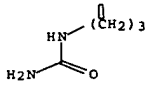

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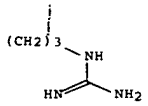

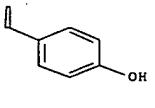

RN 359428-58-3 CAPLUS

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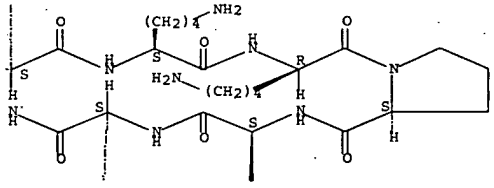
NTE modified

SEQ 1 RRWCYRKKPY RXCR

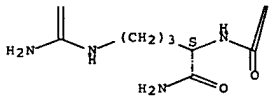
Absolute stereochemistry.

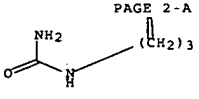
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



PAGE 2-A





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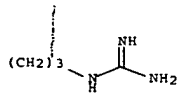
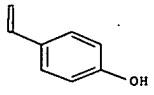




RN 359428-59-4 CAPLUS

CN L-Argininamide, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

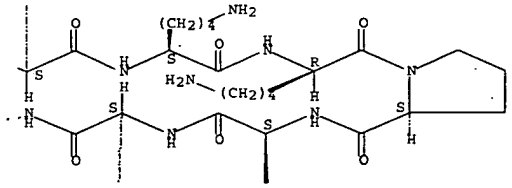
NTE modified

SEQ 1 RRACYRKKPY RXCR

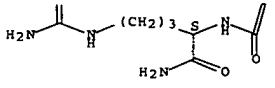
Absolute stereochemistry.

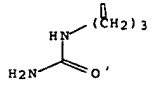
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



PAGE 2-A





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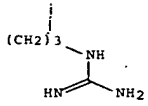
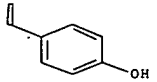




RN 359428-60-7 CAPLUS

CN L-Argininamide, L-arginyl-L-arginyl-S-(phenylmethyl)-L-cysteinyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

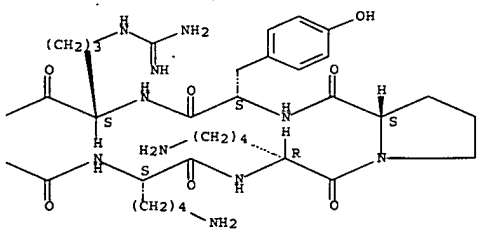
NTE modified

SEQ 1 RRCCYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



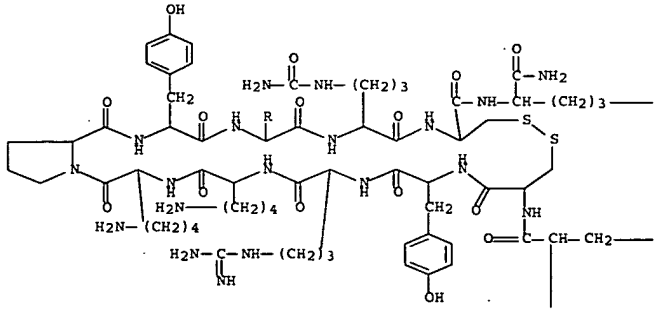
RN 359428-61-8 CAPLUS

CN L-Argininamide, L-arginyl-L-arginyl-S-(tricyclo[3.3.1.13,7]dec-1-ylmethyl)-L-cysteinyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

NTE modified

SEQ 1 RRCCYRKKPY RXCR

PAGE 1-A



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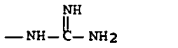

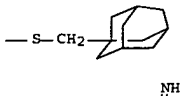

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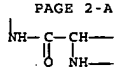

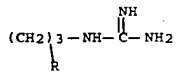

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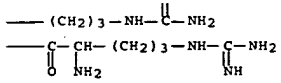


IT 359428-51-6P 359428-52-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyclopeptides and peptide cyclic disulfides as antagonists of CXCR-4 chemokine receptors and antiviral agents, in particular against HIV)

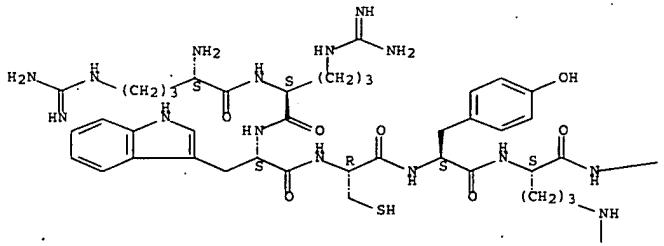
RN 359428-51-6 CAPLUS

CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (9CI) (CA INDEX NAME)

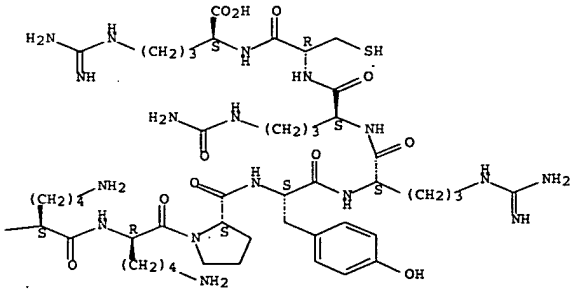
SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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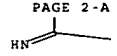


PAGE 2-B

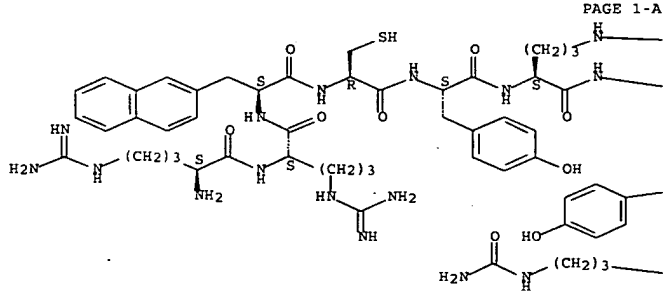
RN 359428-52-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl- (CA INDEX NAME)

NTE modified (modifications unspecified)

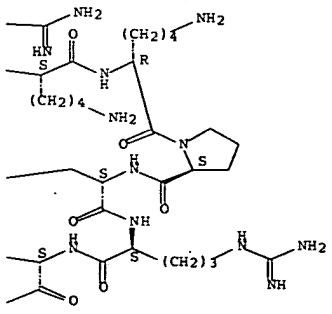
SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

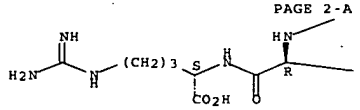
PAGE 1-A



PAGE 1-B



PAGE 2-A



PAGE 2-B

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:629015 CAPLUS Full-text
DOCUMENT NUMBER: 138:265152
TITLE: Conformational study of a highly specific CXCR4 inhibitor, T140, disclosing the close proximity of its intrinsic pharmacophores associated with strong anti-HIV activity. [Erratum to document cited in CA134:305009]
AUTHOR(S): Tamamura, H.; Sugioka, M.; Odagaki, Y.; Omagari, A.; Kan, Y.; Oishi, S.; Nakashima, H.; Yamamoto, N.; Peiper, S. C.; Hamanaka, N.; Otaka, A.; Fujii, N.
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto, 606-8501, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(17), 2409
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 Aug 2001
AB The corrected version of Figure 3 is given.
IT 229030-20-0, T140
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conformational study of highly specific CXCR4 inhibitor T140 disclosing close proximity of intrinsic pharmacophores associated with strong anti-HIV activity (Erratum))
RN 229030-20-0 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

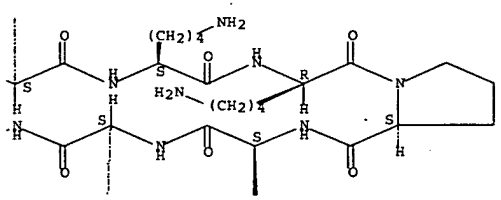
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

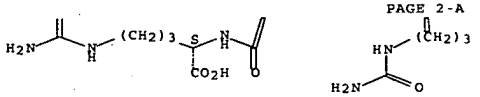
Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

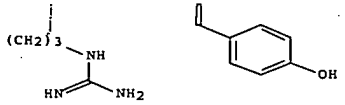
PAGE 1-B



PAGE 2-A



PAGE 2-B



L25 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:591201 CAPLUS Full-text
DOCUMENT NUMBER: 135:358132
TITLE: Synthesis and evaluation of bifunctional anti-HIV agents based on specific CXCR4 antagonists-AZT conjugation
AUTHOR(S): Tamamura, Hirokazu; Omagari, Akane; Hiramatsu,

Kenichi; Kanamoto, Taisei; Gotoh, Kazuyo; Kanbara, Kenji; Yamamoto, Naoki; Nakashima, Hideki; Otaka, Akira; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Sakyo-ku, 606-8501, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(8), 2179-2187
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:358132
ED Entered STN: 15 Aug 2001
AB We have previously found that T140, a 14-amino acid residue peptide, inhibits infection of target cells by T cell-line-tropic strains of HIV-1 (X4-HIV-1) through its specific binding to a chemokine receptor, CXCR4. Here, we report synthesis and evaluation of bifunctional anti-HIV compds., which are composed of T140 analogs and a reverse transcriptase inhibitor, 3'-azido-3'-deoxythymidine (AZT). Novel conjugated analogs have been proved to have the ability for controlled release of AZT in neutral aqueous media as well as mouse and feline sera, and high selectivity indexes (SIs, 50% cytotoxic concentration/50% effective concentration) caused by a synergistic effect of two different regenerating agents. Thus, these bifunctional compds. have several potential advantages. T140 analogs can possibly work as a carrier of AZT targeting T cells due to their specific affinity for CXCR4 on T cells. A synergistic effect by two types of regenerating agents may enable drug dosage to be reduced, and thus it may effectively suppress toxic side effects and the appearance of drug-resistant virus.
IT 371916-88-0P 371916-90-4P 371916-91-5P
371916-92-6P 371916-94-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and evaluation of bifunctional anti-HIV agents based on specific CXCR4 antagonists-AZT conjugation)
RN 371916-88-0 CAPLUS
CN L-Arginine, N2-(3-carboxy-1-oxopropyl)-L-arginyl-L-arginyl-3-(1-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

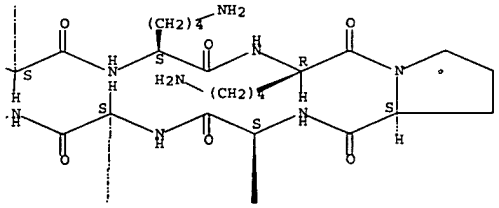
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

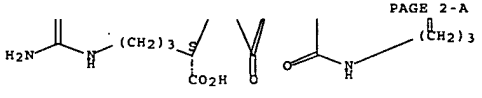
Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

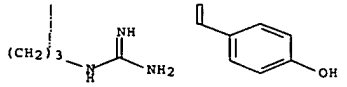
PAGE 1-B



PAGE 2-A



PAGE 2-B



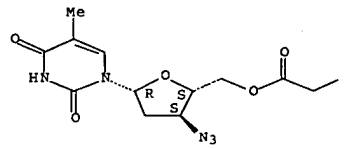
RN 371916-90-4 CAPLUS
CN L-Arginine, N2-(3-carboxy-1-oxopropyl)-L-arginyl-L-arginyl-3-(1-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, 1→5'-ester with 3'-azido-3'-deoxythymidine, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

NTE modified (modifications unspecified)

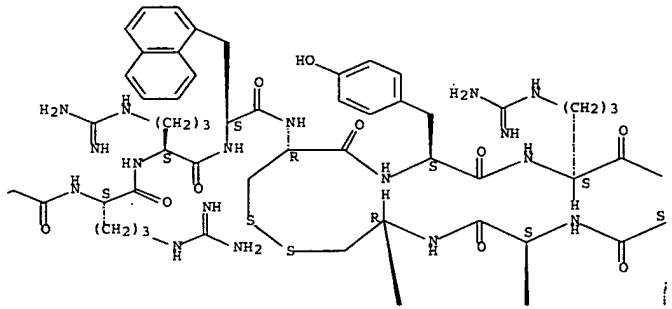
SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



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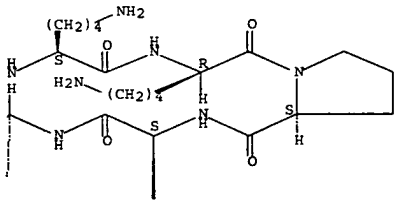
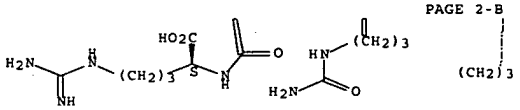


PAGE 2-B



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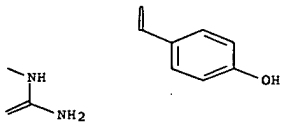


RN 371916-91-5 CAPLUS
CN L-Argininamide, L-arginyl-L-arginyl-3-(1-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

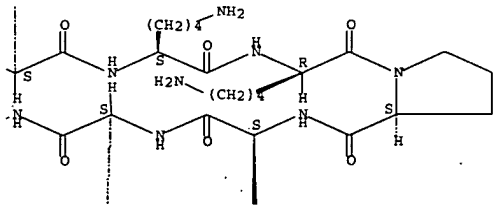
NTE modified

SEQ 1 RRACYRKKPY RXCR

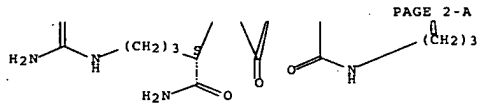
Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

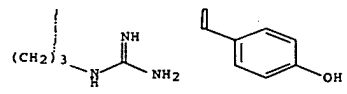
PAGE 1-B



PAGE 2-A



PAGE 2-B



RN 371916-92-6 CAPLUS
CN L-Argininamide, N2-(3-carboxy-1-oxopropyl)-L-arginyl-L-arginyl-3-(1-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

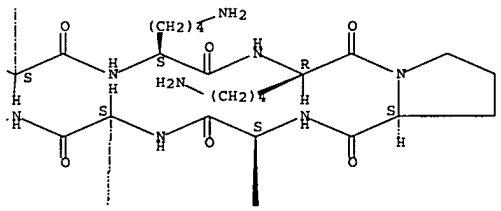
NTE modified

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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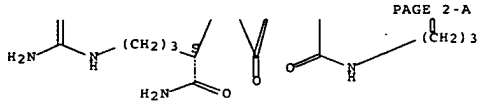

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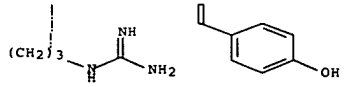

RN 371916-94-8 CAPLUS

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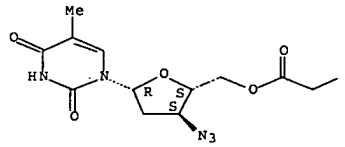
NTE modified

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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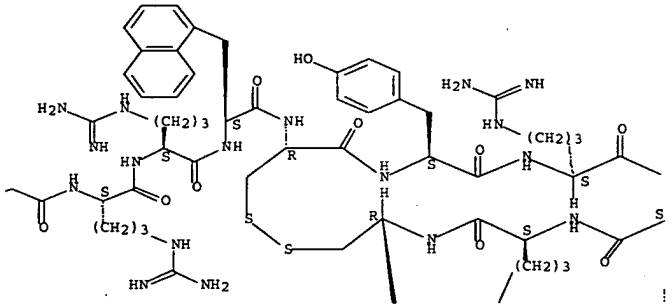

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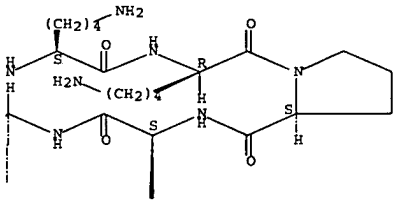

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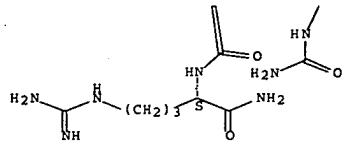

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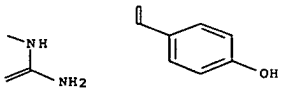

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:518621 CAPLUS Full-text
DOCUMENT NUMBER: 135:313191
TITLE: Development of specific CXCR4 inhibitors possessing high selectivity indexes as well as complete stability in serum based on an anti-HIV peptide T140
AUTHOR(S): Tamamura, H.; Omagari, A.; Hiramatsu, K.; Gotoh, K.; Kanamoto, T.; Xu, Y.; Kodama, E.; Matsuoka, M.; Hattori, T.; Yamamoto, N.; Nakashima, H.; Otaka, A.; Fujii, N.
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto

University, Sakyo-ku, Kyoto, 606-8501, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(14), 1897-1902
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 18 Jul 2001
AB We previously reported a truncated polyphemusin peptide analog, T140, which efficiently inhibits infection of target cells by T-cell line-tropic strains of HIV-1 (X4-HIV-1) through its specific binding to a chemokine receptor, CXCR4. We have found that T140 is not stable in feline serum due to the cleavage of the C-terminal Arg,14 indispensable for anti-HIV activity. On the other hand, a C-terminally amidated analog of T140, TZ14004, has been found to be completely stable in incubation in the serum for 2 days. The C-terminal amide is thought to be needed for stability in serum. However, TZ14004 does not have fairly strong anti-HIV activity, but has relatively strong cytotoxicity, probably due to an increase by +1 charge from total +7 charges of T140. In our previous study, the number of total +6 charges seemed to be a suitable balance between activity and cytotoxicity. In this study, we have conducted a double-L-citrulline (Cit)-scanning study on TZ14004 based on the C-terminally amidated form in due consideration of the total net charges in the whole mol. to find novel effective CXCR4 inhibitors, TN14003 ([Cit6]-T140 with the C-terminal amide) and TC14012 ([Cit6, d-Cit8]-T140 with the C-terminal amide), which possess high selectivity indexes (SIs) and complete stability in feline serum.
IT 229030-20-0 327610-31-1 359428-59-4
368274-31-1 368874-37-7 368874-38-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(development of specific CXCR4 inhibitors possessing high selectivity indexes as well as complete stability in serum based on anti-HIV peptide T140)
RN 229030-20-0 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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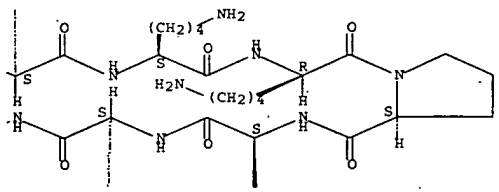

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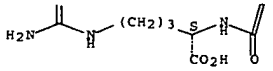

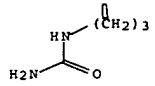

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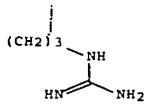

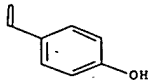

RN 327610-31-1 CAPLUS

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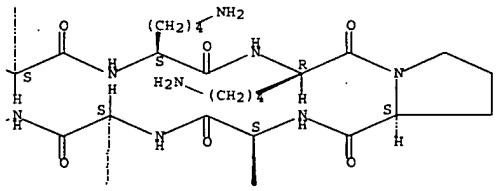
NTE modified (modifications unspecified)

SEQ 1 RRACYXKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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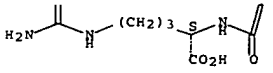

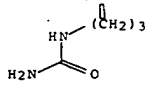

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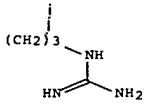

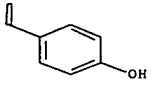

RN 359428-59-4 CAPLUS

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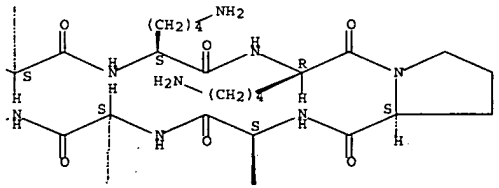
NTE modified

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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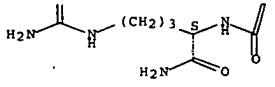

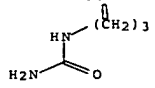

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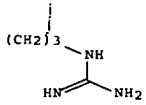

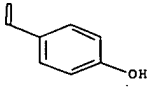

RN 368874-31-1 CAPLUS

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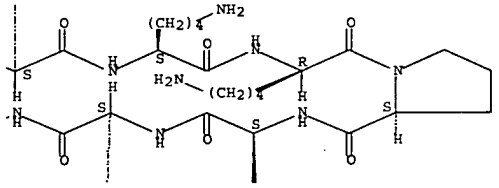
NTE modified

SEQ 1 RRACYXKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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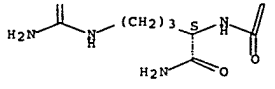

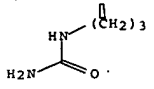

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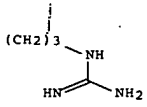

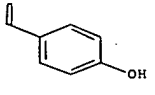

RN 368874-37-7 CAPLUS

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NTE modified (modifications unspecified)

SEQ 1 XRACYXKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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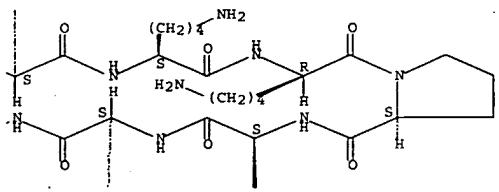

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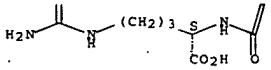

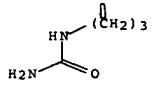

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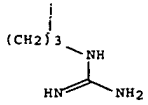

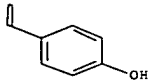

RN 368874-38-8 CAPLUS
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NTE modified

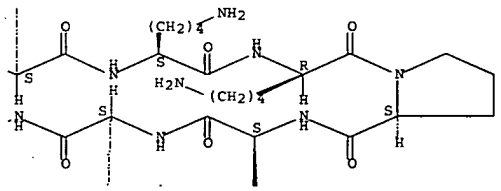
SEQ 1 XRACYXKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

10/525838

PAGE 1-B



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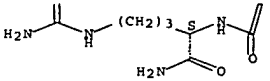

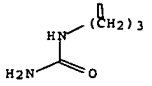

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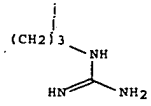
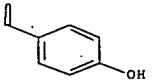




REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:386956 CAPLUS Full-text
DOCUMENT NUMBER: 136:128618
TITLE: Biological and genetic characterization of a human immunodeficiency virus strain resistant to CXCR4 antagonist T134
AUTHOR(S): Kanbara, Kenji; Sato, Setsuko; Tanuma, Jun-Ichi; Tamamura, Hirokazu; Gotoh, Kazuyo; Yoshimori, Manabu; Kanamoto, Taisei; Kitano, Motoo; Fujii, Nobutaka; Nakashima, Hideki
CORPORATE SOURCE: Department of Microbiology and Immunology, Kagoshima University Dental School, Kagoshima, 890-8544, Japan
SOURCE: AIDS Research and Human Retroviruses (2001), 17(7), 615-622

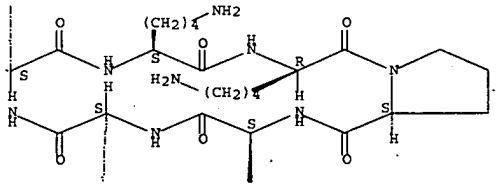
CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 May 2001
AB The chemokine receptors CXCR4 and CCR5 are considered to be potential targets for the inhibition of HIV 1 replication. The authors have reported that T134 and T140 inhibited X4 HIV 1 infection specifically because they acted as CXCR4 antagonists. In the present study, the authors have generated a T134-resistant virus (trHIV-1NL4-3) in a cell culture with gradually increasing concns. of the compound The EC50 of T134 against trHIV-1NL4-3 recovered after 145 passages was 15 times greater than that against wild-type HIV-1NL4-3. This adapted virus was resistant to other CXCR4 antagonists, T140, AMD3100, and ALX40-4C, and SDF-1; from 10 to 145 times greater than that against wild-type HIV-1NL4-3. On the other hand, T134, T140, and ALX40-4C were still active against AMD3100-resistant viruses (arHIV-1018A). The trHIV-1NL4-3 contained the following mutations in the V3 loop of gp120: N269K, Q278T, R279K, A284V, F285L, V286Y, I288T, K290E, N293D, M294I, and Q296K; an insertion of T at 290; and Δ274-275 (SI). In addition, many other mutations were recognized in the V1, V2, and V4 domains. Thus, resistance to T134 may be the consequence of amino acid substitutions in the envelope glycoprotein of X4 HIV 1. The trHIV-1NL4-3 could not utilize CCR5 as an HIV infection coreceptor, although many amino acid substitutions were recognized. The trHIV-1NL4-3 acquired resistance to vMIP II, which could inhibit both X4 and R5 HIV-1 infection. However, neither the ligands of CCR5, RANTES, and MIP-1α, nor a CCR5 low mol. antagonist, TAK-779, were able to influence the infection of trHIV-1NL4-3. Those results indicated that alternation of coreceptor usage of trHIV-1NL4-3 was not induced.
IT 205586-56-7, T134 229030-20-0, T140
RL: PAC (Pharmacological activity); BIOL (Biological study)
(biol. and genetic characterization of human immunodeficiency virus strain resistant to CXCR4 antagonist T134)
RN 205586-56-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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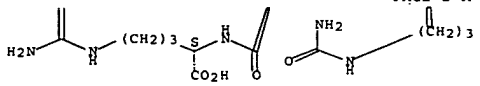

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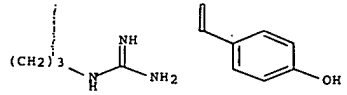

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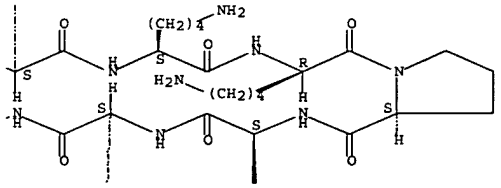
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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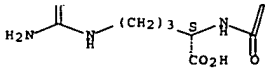

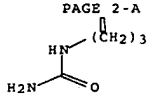

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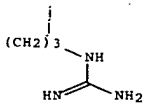
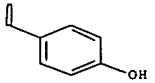




REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:325930 CAPLUS Full-text
DOCUMENT NUMBER: 135:282703
TITLE: Increase of R5 HIV-1 infection and CCR5 expression in T cells treated with high concentrations of CXCR4 antagonists and SDF-1
AUTHOR(S): Gotoh, Kazuyo; Yoshimori, Manabu; Kanbara, Kenji; Tamamura, Hirokazu; Kanamoto, Taisei; Mochizuki, Katsura; Fujii, Nobutaka; Nakashima, Hideki
CORPORATE SOURCE: Department of Microbiology and Immunology, Kagoshima University Dental School, Kagoshima, 890-8544, Japan
SOURCE: Journal of Infection and Chemotherapy (2001), 7(1), 28-36
CODEN: JICHFN; ISSN: 1341-321X

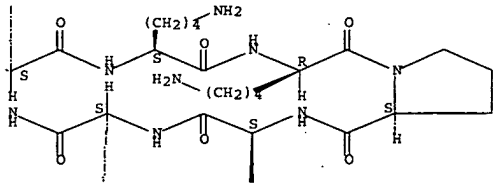
PUBLISHER: Springer-Verlag Tokyo
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 08 May 2001
AB The chemokine receptors CXCR4 and CCR5 are considered to be potential targets for the inhibition of HIV-1 replication. The authors found that the synthetic peptides T134 and T140 (see text for full names) inhibited X4 HIV-1 infection with selectivity and low toxicity because they acted as CXCR4 antagonists. However, high concns. of T134, T140, and ALX40-4C (see text for full name) increased the expression of CCR5 and R5 HIV-1 infection, as did stromal cell-derived factor 1 (SDF-1). In contrast to CXCR4 antagonists and SDF-1, viral monocyte inflammatory protein (vMIP) II inhibited not only anti-CXCR4 monoclonal antibody (MAb) but also inhibited anti-CCR5 MAb binding to human peripheral blood mononuclear cells, and inhibited both X4 and R5 HIV-1 strains. T134, T140, ALX40-4C, and SDF-1 increased viral transcription in the treated cells. In addition, ALX40-4C and SDF-1 also increased nuclear transcription factor (NF)-κB. However, the mechanisms of action of T134 and T140 are different from those of clin. used anti-HIV drugs. Thus, synergistic activities were observed in the concomitant treatment with T134 and reverse transcriptase inhibitors or protease inhibitors. The authors' findings, presented here, are noteworthy in regard to the potential clin. use of these agents as drugs for the treatment of AIDS.
IT 205586-56-7, T134 229030-20-0, T140
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increase of R5 HIV-1 infection and CCR5 expression treated with high concns. of CXCR4 antagonists and SDF-1)
RN 205586-56-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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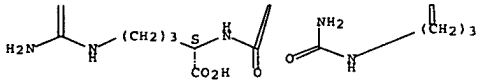

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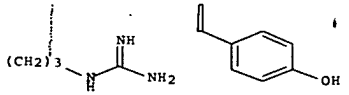

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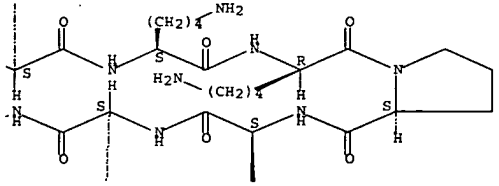
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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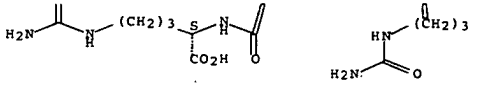

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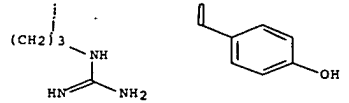

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:311731 CAPLUS Full-text
DOCUMENT NUMBER: 135:251405
TITLE: Development of specific CXCR4 inhibitors based on an anti-HIV peptide, T140, and their structure-activity relationships study
AUTHOR(S): Omagari, Akane; Tamamura, Hirokazu; Oishi, Shinya; Nakashima, Hideki; Otaka, Akira; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Peptide Science (2001), Volume Date 2000, 37th, 129-132
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Japanese Peptide Society

DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 02 May 2001
AB A polyphemusin analog, T22, and its shortened analogs, T134 and T140, strongly inhibit the T-cell line-tropic HIV-1 infection through their specific binding to a chemokine receptor, CXCR4. There is an apparent correlation in the T22-related peptides between the number of total pos. net charges and anti-HIV activity or cytotoxicity. Here, we have conducted the conventional Ala-scanning study in order to define the anti-HIV activity pharmacophore of T140. Based on the result, a series of L-citrulline-substituted analogs of T140 with decreased net pos. charges have been synthesized. As a result, novel effective inhibitors have been developed.
IT 205586-56-7, T134 229030-20-0, T140 327610-17-3
327610-18-4 327610-19-5 327610-20-8
327610-21-9 327610-22-0 327610-24-2
327610-29-7 327610-30-0 327610-31-1
327610-32-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(development of specific CXCR4 inhibitors based on anti-HIV peptide, T140, and structure-activity relationships study)
RN 205586-56-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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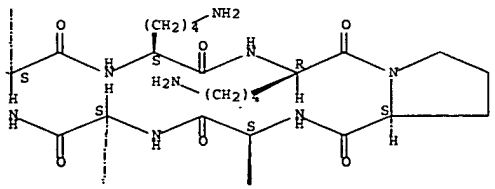

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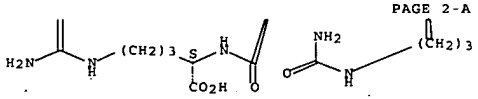

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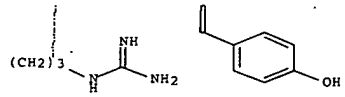

RN 229030-20-0 CAPLUS
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NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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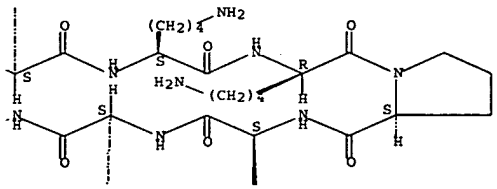

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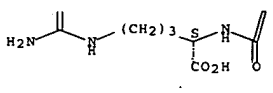

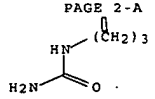

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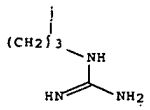

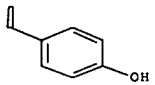

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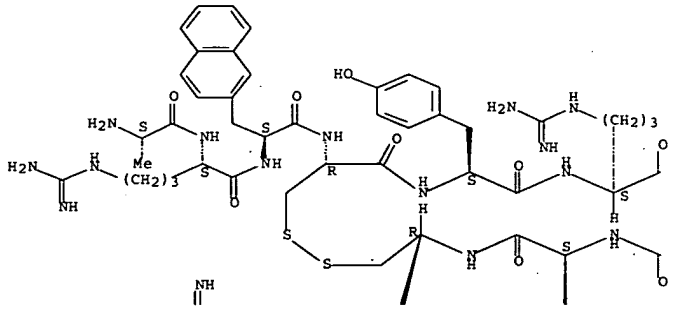
NTE modified (modifications unspecified)

SEQ 1 ARACYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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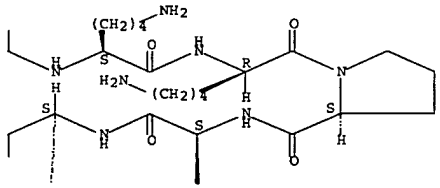

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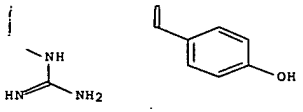
PAGE 2-B



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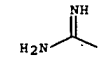
NTE modified

SEQ 1 RAACYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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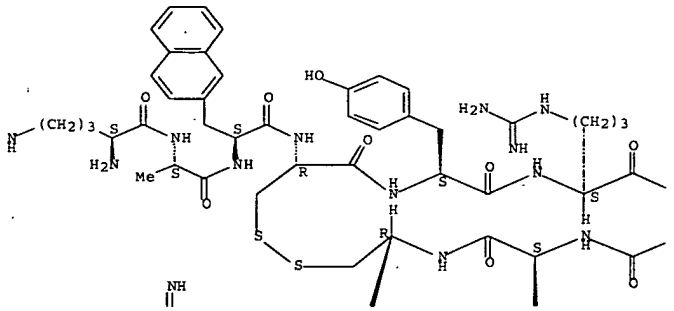

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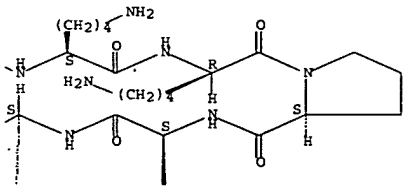

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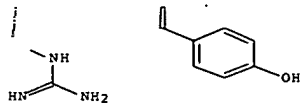

RN 327610-19-5 CAPLUS
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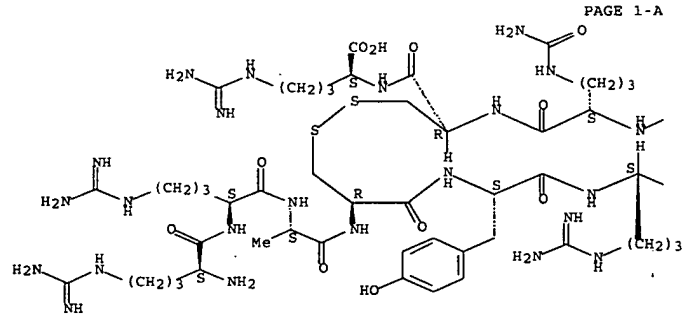
SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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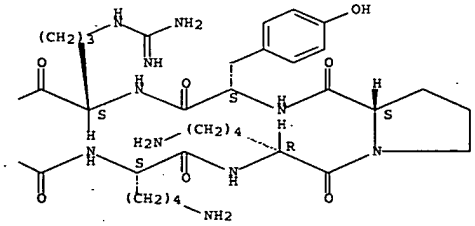

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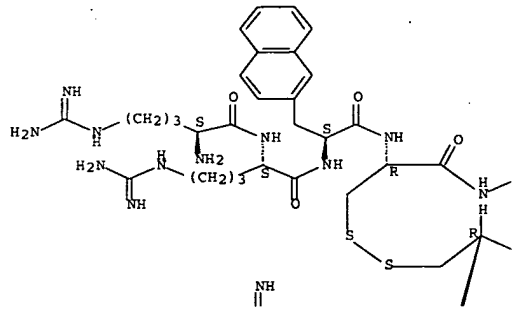
NTE modified

SEQ 1 RRACARKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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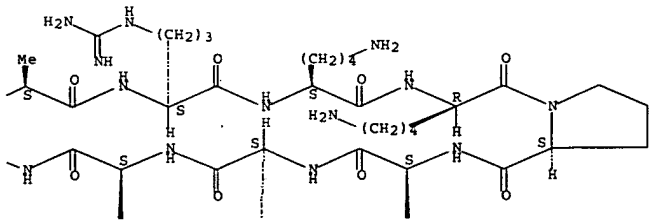

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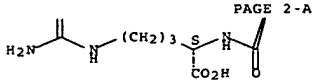

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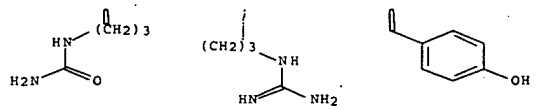


RN 327610-21-9 CAPLUS

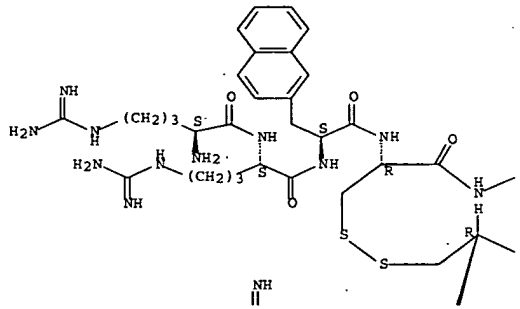
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-alanyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 RRACYAKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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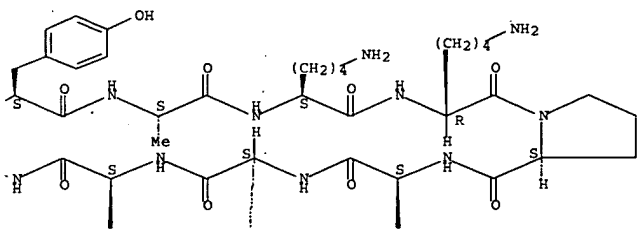

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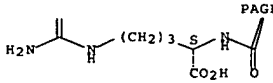

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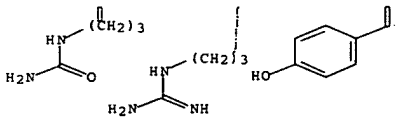

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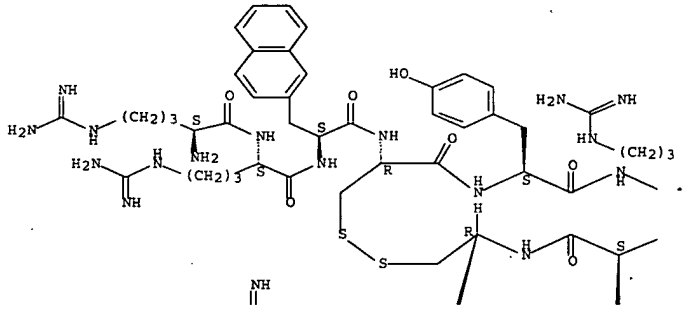
NTE modified (modifications unspecified)

SEQ 1 RRACYRAKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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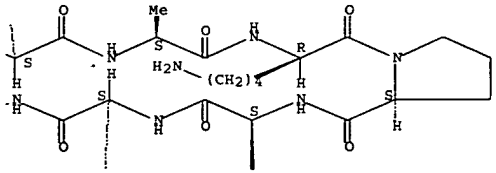

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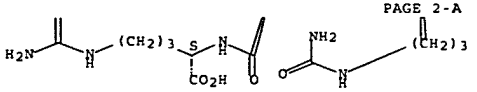

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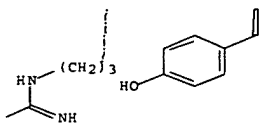

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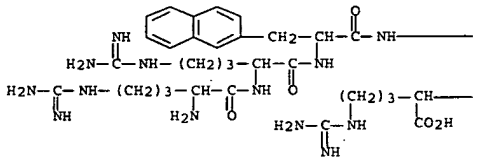
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKAY RXCR

PAGE 1-A



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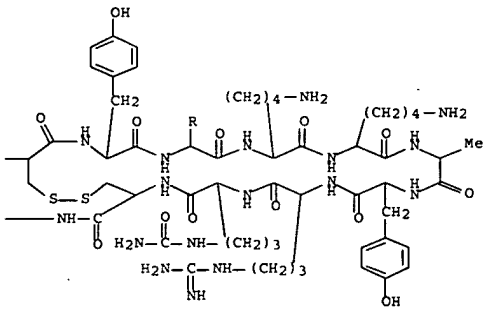

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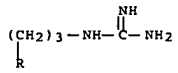

RN 327610-29-7 CAPLUS
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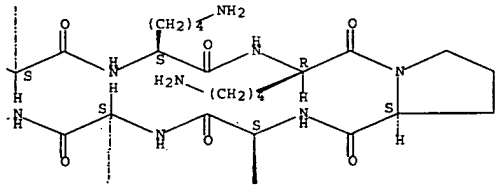
NTE modified (modifications unspecified)

SEQ 1 XRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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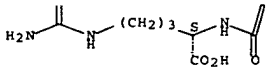

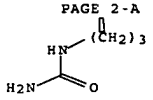

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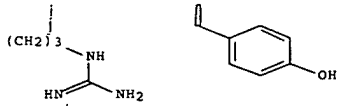

RN 327610-30-0 CAPLUS

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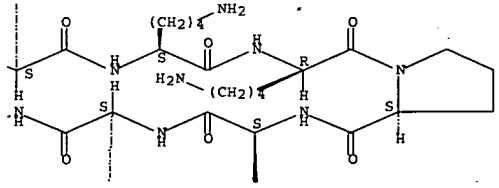
NTE modified

SEQ 1 RXACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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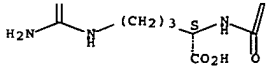

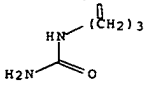

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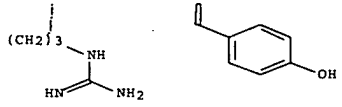

RN 327610-31-1 CAPLUS

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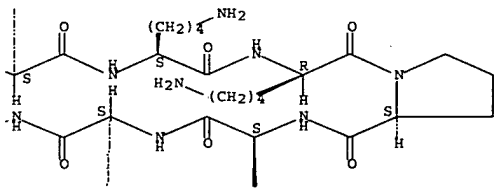
NTE modified (modifications unspecified)

SEQ 1 RRACYXKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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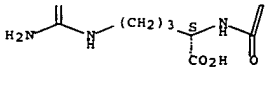

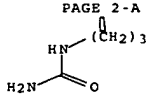

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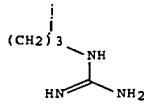

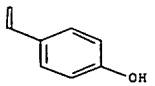

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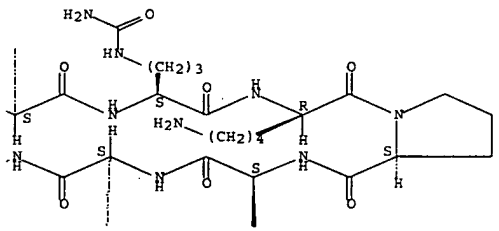
NTE modified (modifications unspecified)

SEQ 1 RRACYRXKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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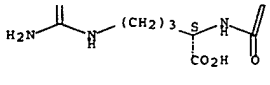

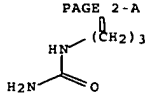

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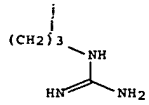
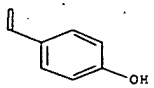




REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:118620 CAPLUS Full-text
DOCUMENT NUMBER: 134:305009
TITLE: Conformational study of a highly specific CXCR4 inhibitor, T140, disclosing the close proximity of its intrinsic pharmacophores associated with strong anti-HIV activity
AUTHOR(S): Tamamura, H.; Sugioka, M.; Odagaki, Y.; Omagari, A.; Kan, Y.; Oishi, S.; Nakashima, H.; Yamamoto, N.; Peiper, S. C.; Hamanaka, N.; Otaka, A.; Fujii, N.
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Sakyo-ku, 606-8501, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(3), 359-362

CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 18 Feb 2001
AB The authors report the solution structure of T140, a truncated polyphemusin peptide analog that efficiently inhibits infection of target cells by T-cell line-tropic strains of HIV-1 through its specific binding to a chemokine receptor, CXCR4. NMR anal. and mol. dynamic calcns. revealed that T140 has a rigidly structured conformation constituted by an antiparallel β-sheet and a type II' β-turn. A protuberance is formed on one side of the β-sheet by the side-chain functional groups of the three amino acid residues (1-3-(2-naphthyl)alanine3, Tyr5 and Arg14), each of which is indispensable for strong anti-HIV activity. These findings provide a rationale to dissect the structural basis for the ability of this compound to block the interaction between CXCR4 and envelope glycoproteins from T-tropic strains of HIV-1.
IT 229030-20-0, T140
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conformational study of highly specific CXCR4 inhibitor T140 disclosing close proximity of intrinsic pharmacophores associated with strong anti-HIV activity)
RN 229030-20-0 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

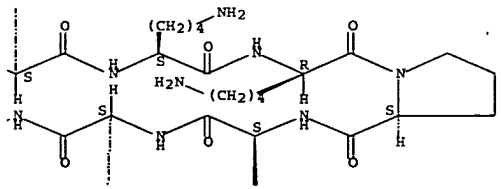
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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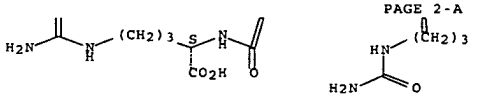

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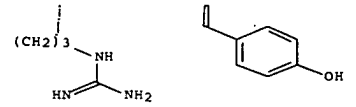


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:832460 CAPLUS Full-text
DOCUMENT NUMBER: 134:187820
TITLE: Pharmacophore identification of a specific CXCR4 inhibitor, T140, leads to development of effective anti-HIV agents with very high selectivity indexes
AUTHOR(S): Tamamura, H.; Omagari, A.; Oishi, S.; Kanamoto, T.; Yamamoto, N.; Peiper, S. C.; Nakashima, H.; Otaka, A.; Fujii, N.
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto, 606-8501, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(23), 2633-2637
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 29 Nov 2000
AB A polyphemusin peptide analog, T22 ([Tyr5,12, Lys7]-polyphemusin II), and its shortened potent analogs, T134 (des-[Cys8,13, Tyr9,12]-[d-Lys10, Pro11, 1-citrulline16]-T22 without C-terminal amide) and T140 {[1-3-(2-naphthyl)alanine3]-T134}, strongly inhibit the T-cell line-tropic (T-tropic) HIV-1 infection through their specific binding to a chemokine receptor, CXCR4. T22 is an extremely basic peptide possessing five Arg and three Lys residues in the mol. In our previous study, we found that there is an apparent correlation in the T22-related peptides between the number of total pos. charges and anti-HIV activity or cytotoxicity. Here, we have conducted the conventional Ala-scanning study to define the anti-HIV activity pharmacophore of T140 (the strongest analog among our compds.) and identified four indispensable amino acid residues (Arg2, Nal3, Tyr5, and Arg14). Based on this result, a series of 1-citrulline (Cit)-substituted analogs of T140 with decreased net pos. charges have been synthesized and evaluated in terms of anti-HIV activity and cytotoxicity. As a result, novel effective inhibitors, TC14003 and TC14005, possessing higher selectivity indexes (SIs, 50% cytotoxic

concentration/50% effective concentration) than that of T140 have been developed.

IT 327610-17-3P 327610-18-4P 327610-19-5P
327610-20-8P 327610-21-9P 327610-22-0P
327610-24-2P 327610-29-7P 327610-30-0P
327610-31-1P 327610-32-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmacophore identification of a specific CXCR4 inhibitor, T140, and preparation of anti-HIV agents with high selectivity indexes)

RN 327610-17-3 CAPLUS

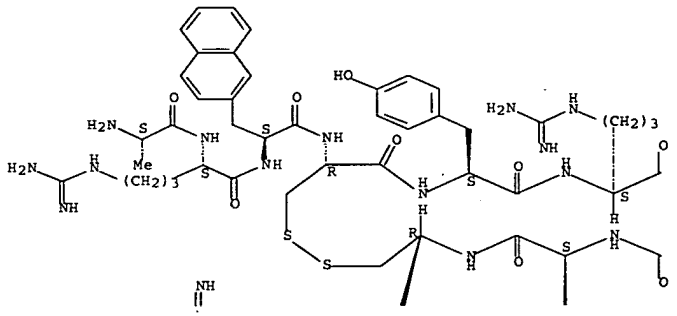
CN L-Arginine, L-alanyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

NTE modified (modifications unspecified)

SEQ 1 ARACYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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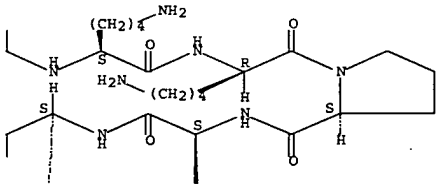
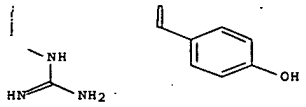


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 2-B



RN 327610-18-4 CAPLUS

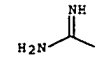
CN L-Arginine, L-arginyl-L-alanyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

NTE modified

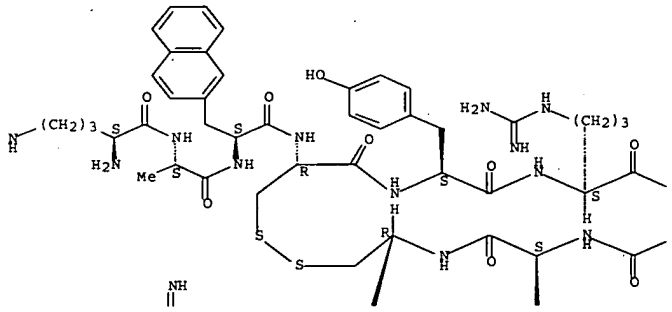
SEQ 1 RAACYRKKPY RXCR

Absolute stereochemistry.

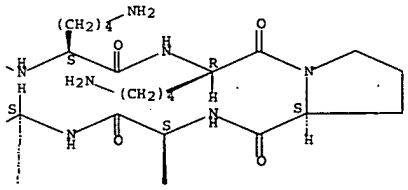
PAGE 1-A



PAGE 1-B

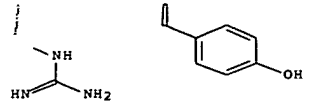


PAGE 1-C



*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

PAGE 2-C

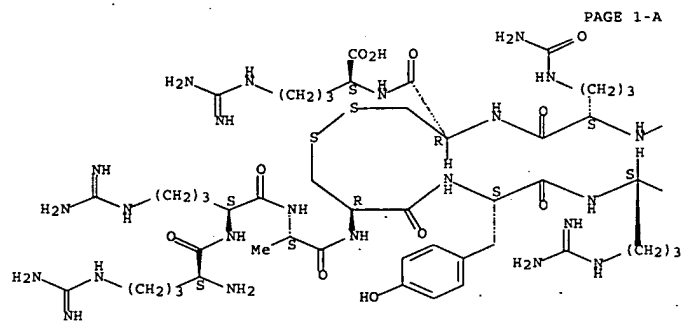


RN 327610-19-5 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

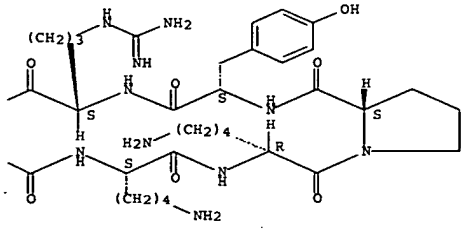
SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 327610-20-8 CAPLUS
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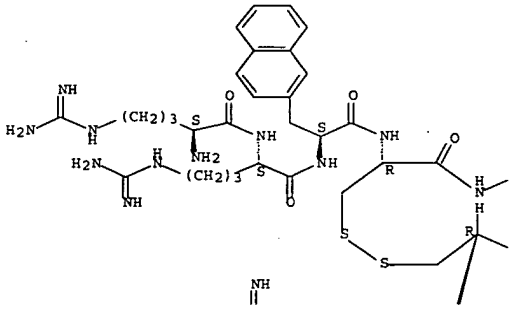
NTE modified

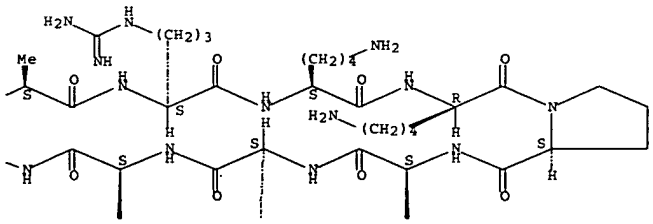
SEQ 1 RRACARKKPY RXCR

Absolute stereochemistry.

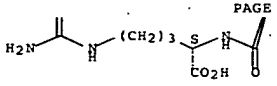
PAGE 1-A



PAGE 1-B



PAGE 2-A



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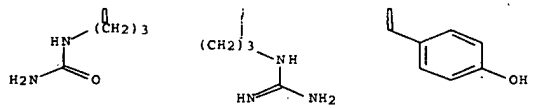


RN 327610-21-9 CAPLUS

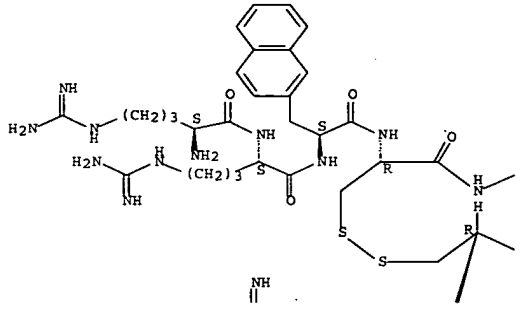
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-alanyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

NTE modified (modifications unspecified)

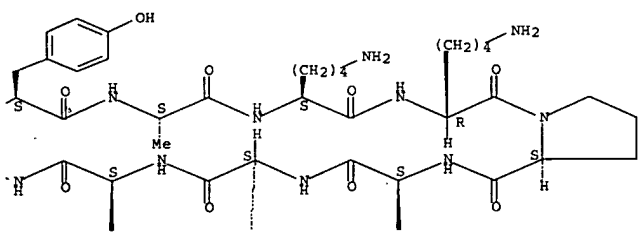
SEQ 1 RRACYAKKPY RXCR

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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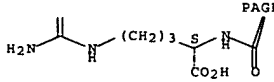

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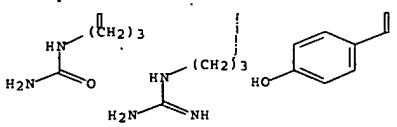

RN 327610-22-0 CAPLUS
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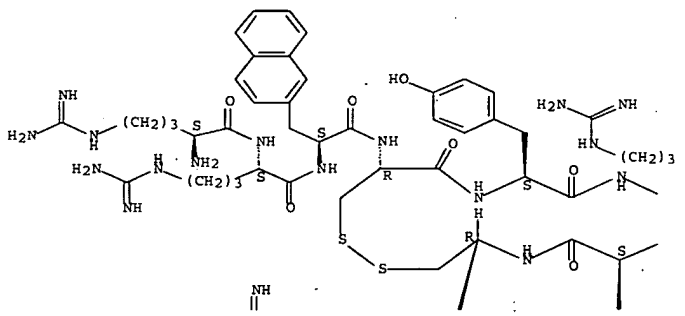
NTE modified (modifications unspecified)

SEQ 1 RRACYRAKPY RXCR

Absolute stereochemistry.

PAGE 1-A



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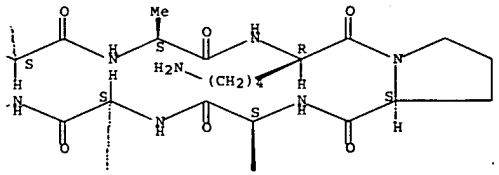

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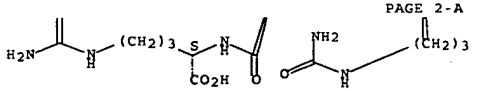

H2N

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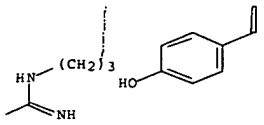

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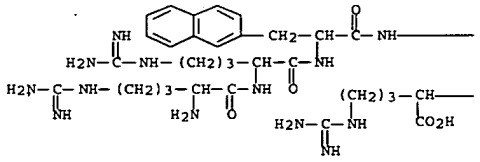
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKAY RXCR

PAGE 1-A



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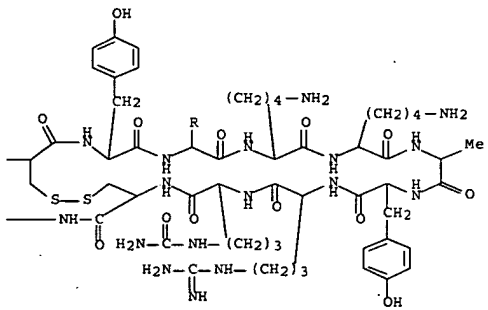

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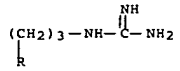


RN 327610-29-7 CAPLUS
CN L-Arginine, N5-(aminocarbonyl)-L-ornithyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

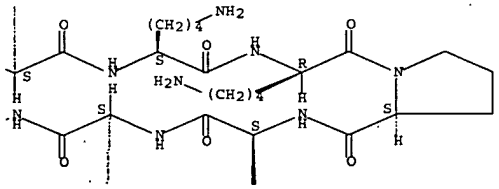
NTE modified (modifications unspecified)

SEQ 1 XRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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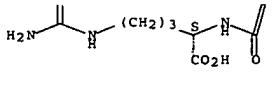

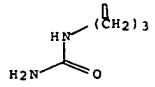

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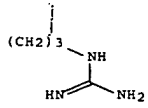

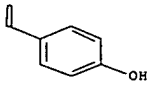

RN 327610-30-0 CAPLUS

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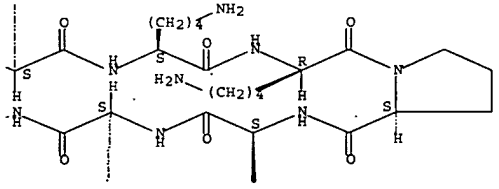
NTE modified

SEQ 1 RXACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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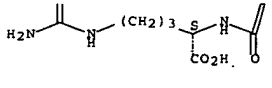

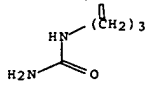

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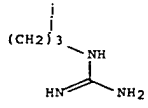
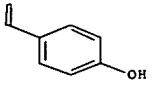




RN 327610-31-1 CAPLUS

CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

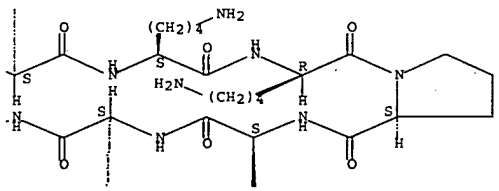
NTE modified (modifications unspecified)

SEQ 1 RRACYXKKPY RXCR

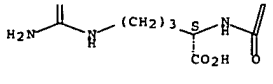
Absolute stereochemistry.

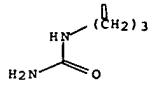
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



PAGE 2-A





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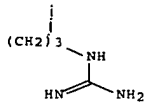
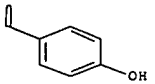




RN 327610-32-2 CAPLUS

CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

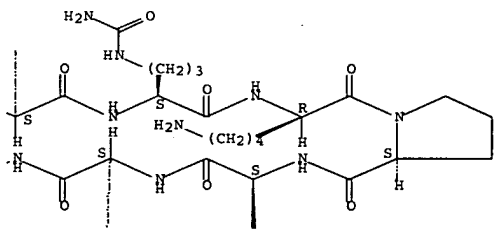
NTE modified (modifications unspecified)

SEQ 1 RRACYRXKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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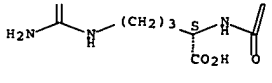

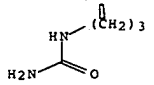

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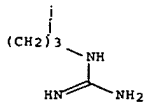
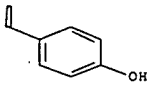




IT 205586-56-7, T134 229030-20-0, T140

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmacophore identification of a specific CXCR4 inhibitor, T140, and preparation of anti-HIV agents with high selectivity indexes)

RN 205586-56-7 CAPLUS

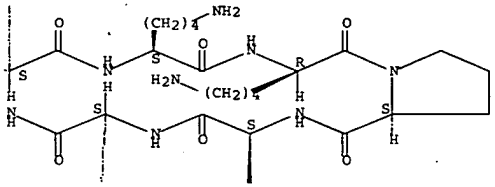
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

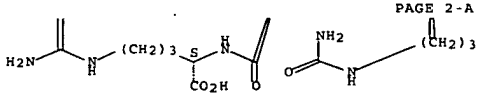
Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



PAGE 2-A



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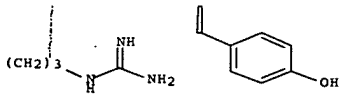


RN 229030-20-0 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

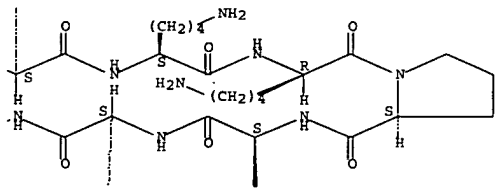
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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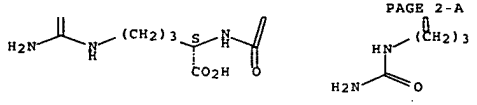

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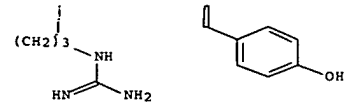


REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:288668 CAPLUS Full-text
DOCUMENT NUMBER: 133:164303
TITLE: Ring-closing metathesis produced a CXCR4 antagonist with anti-HIV activity
AUTHOR(S): Hirohashi, Mariko; Tamamura, Hirokazu; Otaka, Akira; Ibuka, Toshiro; Arakaki, Rieko; Nakashima, Hideki; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Japan
SOURCE: Peptides 1998, Proceedings of the European Peptide

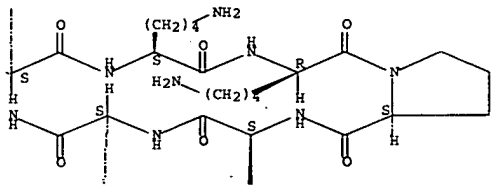
Symposium, 25th, Budapest, Aug. 30-Sept. 4, 1998 (1999), Meeting Date 1998, 662-663. Editor(s): Bajusz, Sandor; Hudecz, Ferenc. Akademiai Kiado: Budapest, Hung.
CODEN: 68WKAY
DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 04 May 2000
AB A symposium report. Ru-catalyzed ring-closing metathesis (RCM) was applied to replacement of a disulfide bridge with a carbon-carbon double bond, e.g., in anti-HIV peptide T134. Anti-HIV activities of the products are tabulated.
IT 205586-56-7P, t134 229030-20-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(ring-closing metathesis for preparation of CXCR4 antagonist with anti-HIV activity)
RN 205586-56-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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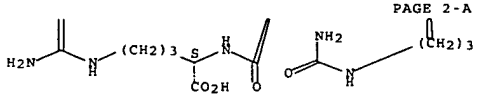

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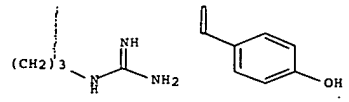


RN 229030-20-0 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

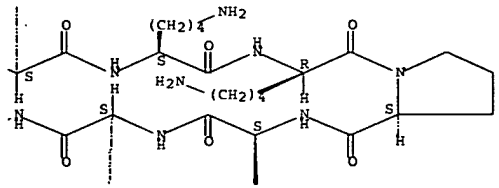
NTE modified (modifications unspecified)

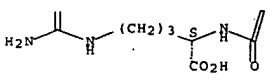
SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B





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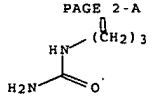

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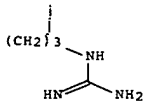

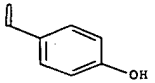

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:264482 CAPLUS Full-text
DOCUMENT NUMBER: 133:105303
TITLE: Application of ring closing olefin metathesis to the conformational restriction of biologically active peptide. Part 1
AUTHOR(S): Fujii, Nobutaka; Hirohashi, Mariko; Oishi, Shinya; Akaji, Masako; Omagari, Akane; Otaka, Akira; Ibuka, Toshiro
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Peptide Science (1999), 36th, 193-194
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Japanese Peptide Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Apr 2000
AB A symposium report. Ru-catalyzed ring-closing metathesis (RCM) reaction was applied to the conformational restriction of peptidic CXCR4-chemokine receptor antagonist T22 and its down-sized analogs.
IT 205586-56-7, t134 229030-20-0, t140
RL: RCT (Reactant); RACT (Reactant or reagent)
(ring closing olefin metathesis applied to conformational restriction of peptidic CXCR4-chemokine receptor antagonists)
RN 205586-56-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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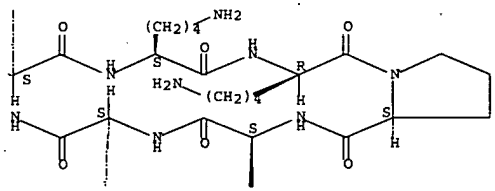

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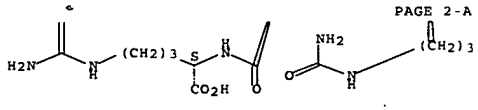

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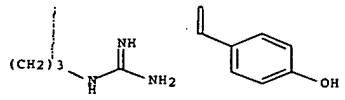


RN 229030-20-0 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

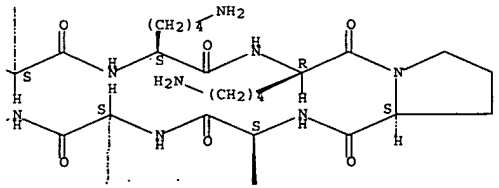
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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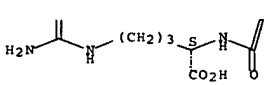

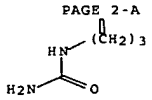

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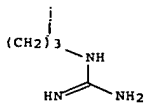
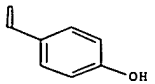




REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:353222 CAPLUS Full-text
DOCUMENT NUMBER: 131:179281
TITLE: HIV-cell fusion inhibitors targeted to the HIV second receptor: T22 and its downsized analogs with high activity
AUTHOR(S): Tamamura, Hirokazu; Omagari, Akane; Murakami, Tsutomu; Arakaki, Rieko; Xu, Younong; Hattori, Toshio; Waki, Michinori; Matsumoto, Akiyoshi; Nakashima, Hideki; Yamamoto, Naoki; Otaka, Akira; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Peptide Science (1999), Volume Date 1998,

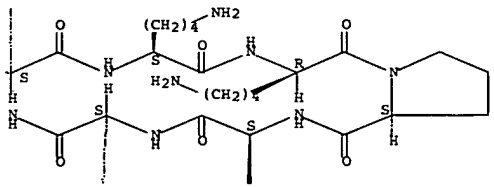
35th, 49-52
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Protein Research Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 09 Jun 1999
AB T22 ([Tyr5,12, Lys7]-polyphemusin II) is an 18-residue peptide amide, which has strong anti-HIV activity. T22 inhibits the T cell line-tropic (T-tropic) HIV-1 infection through its specific binding to CXCR4 (a CXC-chemokine receptor: the second receptor for the entry of T-tropic HIV-1). Herein, we have found novel small-sized effective CXCR4 inhibitors, such as T140 (14 residues). Furthermore, our present SAR study suggests that, in the T22-related analogs, there is a significant correlation between anti-HIV activity and inhibitory activity against HIV entry mediated by CXCR4, and that a remarkable increase in anti-HIV activity of the T22-related analogs results from an enhancement in their binding ability to CXCR4.
IT 205586-56-7P, T134 229030-20-0P, T 140
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HIV-cell fusion inhibitors targeted to the HIV second receptor: anti-HIV activity of the T22-related analogs)
RN 205586-56-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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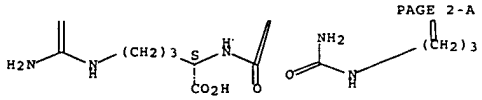

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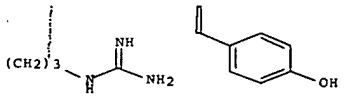


RN 229030-20-0 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

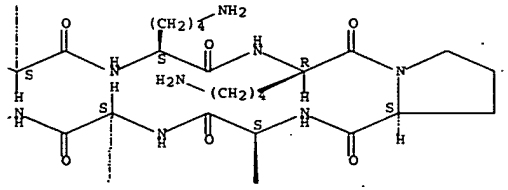
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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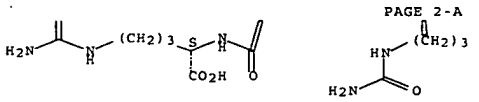

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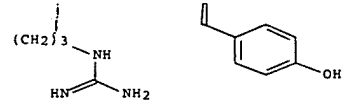


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:227242 CAPLUS Full-text
DOCUMENT NUMBER: 131:67676
TITLE: Marked increase in anti-HIV activity, as well as inhibitory activity against HIV entry mediated by CXCR4, linked to enhancement of the binding ability of tachyplesin analogs to CXCR4
AUTHOR(S): Xu, Younong; Tamamura, Hirokazu; Arakaki, Rieko; Nakashima, Hideki; Zhang, Xiaoyan; Fujii, Nobutaka; Uchiyama, Takashi; Hattori, Toshio
CORPORATE SOURCE: Laboratory of Virus Immunology, Research Center for Acquired Immunodeficiency Syndrome, Institute for Virus Research, Kyoto University, Kyoto, 606-8507, Japan
SOURCE: AIDS Research and Human Retroviruses (1999), 15(5), 419-427
CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 13 Apr 1999
AB T22 ([Tyr5,12, Lys7]-polyphemusin II) is a strong anti-HIV compound Six analogs of T22 and two natural forms were synthesized. Of them, all downsized peptides (14 residues; TW70, T131, T134, and T140) showed a higher selectivity index than did other, 17- or 18-residue peptides. In particular, T134 and T140 showed both lower cytotoxicity and higher antiviral activity than did T22 against HIV infection of MT-4 cells, an HTLV-I-bearing T cell line. To clarify the inhibitory mode of T22 and its analogs, the authors used a single-round replication assay (luciferase assay), in which different envelope-bearing pseudotypes were used to infect CXCR4- or CCR5-bearing U87 cells via CD4. All of the analogs inhibited T cell line-tropic strain HXB-2 (X4) and dual-tropic strain 89.6 (R5X4) HIV infections mediated by CXCR4, but had no effect on macrophage-tropic strain ADA (R5) or 89.6 HIV infections mediated by CCR5. The inhibition by T134 (IC50 of 2.70 nM) and T140 (IC50 of 0.432 nM) was also stronger than that by T22 (IC50 of 5.05 nM). The binding of anti-CXCR4 monoclonal antibody 12G5 to lymphoma-derived T cell line Sup-T1 was more efficiently blocked by T134 and T140 than by T22. Taken together, T22 and its

analogs T134 and T140 exerted their inhibition by specific binding to CXCR4. The marked increase in the anti-HIV activity of T134 and T140 was ascribed to an enhancement in their ability to bind to CXCR4.

IT 205586-56-7, T134 229030-20-0, T 140
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(marked increase in anti-HIV activity as well as inhibitory activity against HIV entry mediated by CXCR4 linked to enhancement of binding ability of tachyplesin analogs to CXCR4)

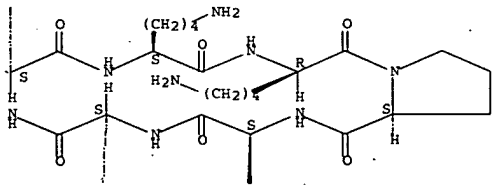
RN 205586-56-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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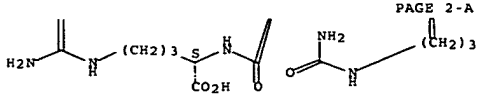

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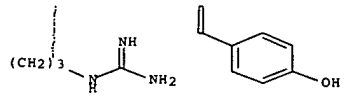


RN 229030-20-0 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-3-(2-naphthalenyl)-L-alanyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (CA INDEX NAME)

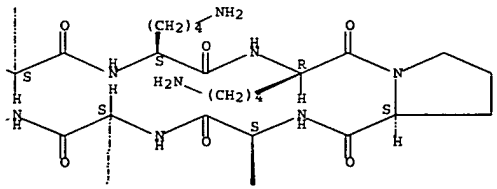
NTE modified (modifications unspecified)

SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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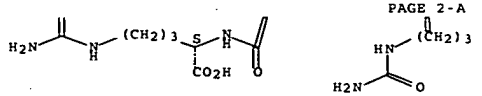

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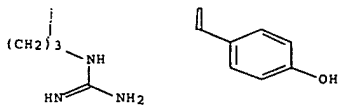


REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

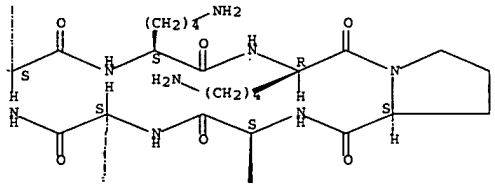
L25 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:63268 CAPLUS Full-text
DOCUMENT NUMBER: 130:261494
TITLE: T134, a small-molecule CXCR4 inhibitor, has no cross-drug resistance with AMD3100, a CXCR4 antagonist with a different structure
AUTHOR(S): Arakaki, Rieko; Tamamura, Hirokazu; Premanathan, Mariappan; Kanbara, Kenji; Ramanan, Sivasundaram; Mochizuki, Katsura; Baba, Masanori; Fujii, Nobutaka; Nakashima, Hideki
CORPORATE SOURCE: Department of Microbiology and Immunology, Kagoshima University Dental School, Kagoshima, 890-8544, Japan
SOURCE: Journal of Virology (1999), 73(2), 1719-1723
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 01 Feb 1999
AB T22, an analog of polyphemusin II (18 amino acid residues), was found to block T-tropic human immunodeficiency virus type 1 (HIV-1) entry into target cells as a CXCR4 inhibitor. We synthesized T134, a small analog (14 amino acid residues) of T22 with reduced pos. charges. T134 exhibited highly potent activity and significantly less cytotoxicity in comparison to that of T22. T134 prevents the anti-CXCR4 monoclonal antibody from binding to peripheral blood mononuclear cells but has no effect on the binding of anti-CCR5 monoclonal antibodies. Since T134 inhibits the binding of stromal cell-derived factor-1 (SDF-1) to MT-4 cells, it seems that T134 prevents HIV-1 entry by binding to CXCR4. The bicyclam AMD3100 has also been shown to block HIV-1 entry via CXCR4 but not via CCR5. Both T134 and AMD3100 are CXCR4 antagonists and low-mol. weight compds. but have different structures. Our results indicate that T134 is active against wild-type T-tropic HIV-1 strains and against AMD3100-resistant strains.
IT 205586-56-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CXCR4 inhibitor T134 lacking cross-drug resistance with AMD3100)
RN 205586-56-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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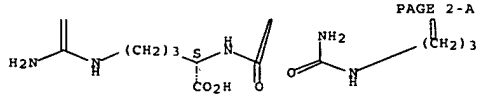

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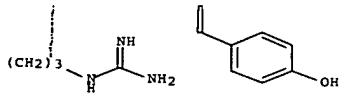


REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:36544 CAPLUS Full-text
DOCUMENT NUMBER: 130:231956
TITLE: A low-molecular-weight inhibitor against the chemokine receptor CXCR4: a strong anti-HIV peptide T140
AUTHOR(S): Tamamura, Hirokazu; Xu, Younong; Hattori, Toshio; Zhang, Xiaoyan; Arakaki, Rieko; Kanbara, Kenji; Omagari, Akane; Otaka, Akira; Ibuka, Toshiro; Yamamoto, Naoki; Nakashima, Hideki; Fujii, Nobutaka

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SOURCE: Biochemical and Biophysical Research Communications (1998), 253(3), 877-882
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 20 Jan 1999

AB T22 ([Tyr5,12, Lys7]-polyphemusin II) is an 18-residue peptide amide, which has strong anti-HIV activity. T22 inhibits the T cell line-tropic (T-tropic) HIV-1 infection through its specific binding to a chemokine receptor CXCR4, which serves as a coreceptor for the entry of T-tropic HIV-1 strains. Herein, we report our finding of novel 14-residue CXCR4 inhibitors, T134 and T140, on the basis of the T22 structure. In the assays we examined, T140 showed the highest inhibitory activity against HIV-1 entry and the strongest inhibitory effect on the binding of an anti-CXCR4 monoclonal antibody (12G5) to CXCR4 among all the CXCR4 inhibitors that have been reported up to now. (c) 1998 Academic Press.

IT 221351-48-0 221351-50-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-HIV peptide T140 and analogs as inhibitors against chemokine receptor CXCR4)

RN 221351-48-0 CAPLUS
CN L-Argininamide, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-D-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

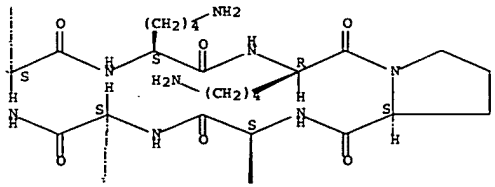
NTE modified

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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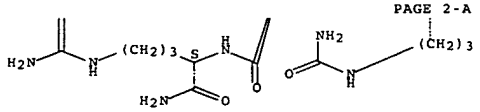

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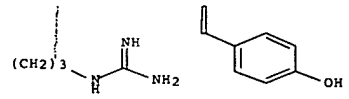

RN 221351-50-4 CAPLUS
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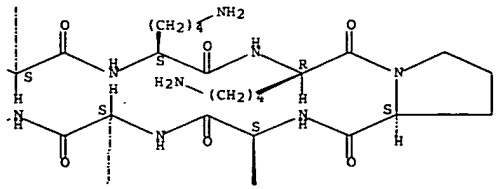
NTE modified

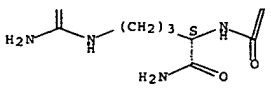
SEQ 1 RRACYRKKPY RXCR

Absolute stereochemistry.

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B





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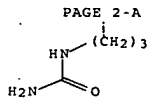

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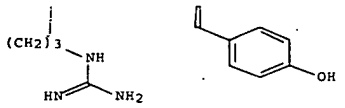


REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:168442 CAPLUS Full-text
DOCUMENT NUMBER: 128:265787
TITLE: Effective lowly cytotoxic analogs of an HIV-cell fusion inhibitor, T22 ([Tyr5,12, Lys7]-polyphemusin II)
AUTHOR(S): Tamamura, Hirokazu; Arakaki, Rieko; Funakoshi, Hanae; Imai, Makoto; Otaka, Akira; Ibuka, Toshiro; Nakashima, Hideki; Murakami, Tsutomu; Waki, Michinori; Matsumoto, Akiyoshi; Yamamoto, Naoki; Fujii, Nobutaka
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-01, Japan
SOURCE: Bioorganic & Medicinal Chemistry (1998), 6(2), 231-238
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 21 Mar 1998
AB A tachyplesin peptide analog, T22 ([Tyr5,12, Lys7]-polyphemusin II), and its shortened congener, TW70 (des-[Cys8,13, Tyr9,12]-[D-Lys10, Pro11]-T22) have strong anti-human immunodeficiency virus (HIV) activity, comparable to that of 3'-azido-2', 3'-dideoxythymidine (AZT). T22 and TW70 are extremely basic peptides, containing 5 Arg residues and 3 Lys residues. The number of pos. charges might be related in part to high collateral cytotoxicities of T22 and TW70. Here we have synthesized several analogs, in which the number of pos. charges has been reduced through amino acid substitutions using Glu or L-citrulline. As a result, several effective compds. have been found which possess higher selectivity indexes (SIs, 50% cytotoxic concentration/50% effective concentration) than those of T22 and TW70. Higher SIs were attributed mainly to a decrease in cytotoxicity.
IT 205586-56-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

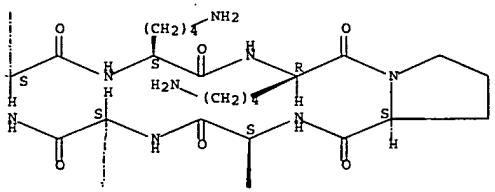
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tachyplesin peptide T22 and TW70 analogs with low cytotoxicity as HIV-cell fusion inhibitors)
RN 205586-56-7 CAPLUS
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-lysyl-D-lysyl-L-prolyl-L-tyrosyl-L-arginyl-N5-(aminocarbonyl)-L-ornithyl-L-cysteinyl-, cyclic (4→13)-disulfide (9CI) (CA INDEX NAME)

SEQ 1 RRWCYRKKPY RXCR

Absolute stereochemistry. Rotation (-).

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 1-B



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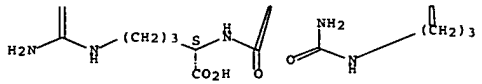

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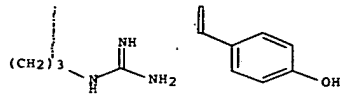

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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SEARCH HISTORY

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

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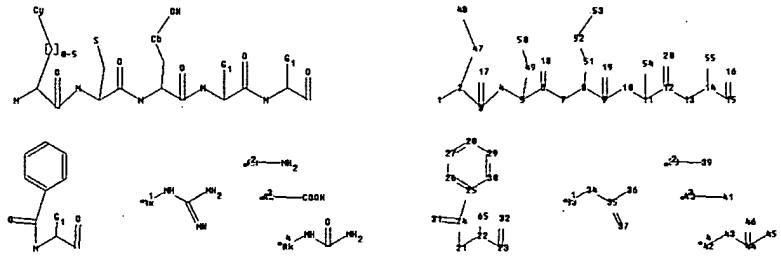

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ring nodes :
25 26 27 28 29 30
ring/chain nodes :
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chain bonds :
1-2 2-3 2-47 3-4 3-17 4-5 6-18 8-51 9-19 11-54 12-20 14-55 15-16 21-22 21-24 22-23 22-65 23-32 24-25 24-31 33-34 34-35 35-36 35-37 38-39 40-41 42-43 43-44 44-45 44-46 47-48 51-52 52-53
ring/chain bonds :
5-6 5-49 6-7 7-8 8-9 9-10 10-11 11-12 12-13 13-14 14-15 49-50
ring bonds :
25-26 25-30 26-27 27-28 28-29 29-30
exact/norm bonds :
1-2 3-4 3-17 4-5 5-6 5-49 6-7 6-18 7-8 8-9 9-10 9-19 10-11 11-12 11-54 12-13 12-20 13-14 14-15 14-55 15-16 21-22 21-24 22-65 23-32 24-31 33-34 34-35 35-36 35-37 38-39 40-41 42-43 43-44 44-45 44-46 47-48 49-50
exact bonds :
2-3 2-47 8-51 22-23 24-25 51-52 52-53
normalized bonds :
25-26 25-30 26-27 27-28 28-29 29-30

G1:CH3,[*1],[*2],[*3],[*4]

Connectivity :
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Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS

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L9               ANALYZE L8 1- LC :       6 TERMS
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